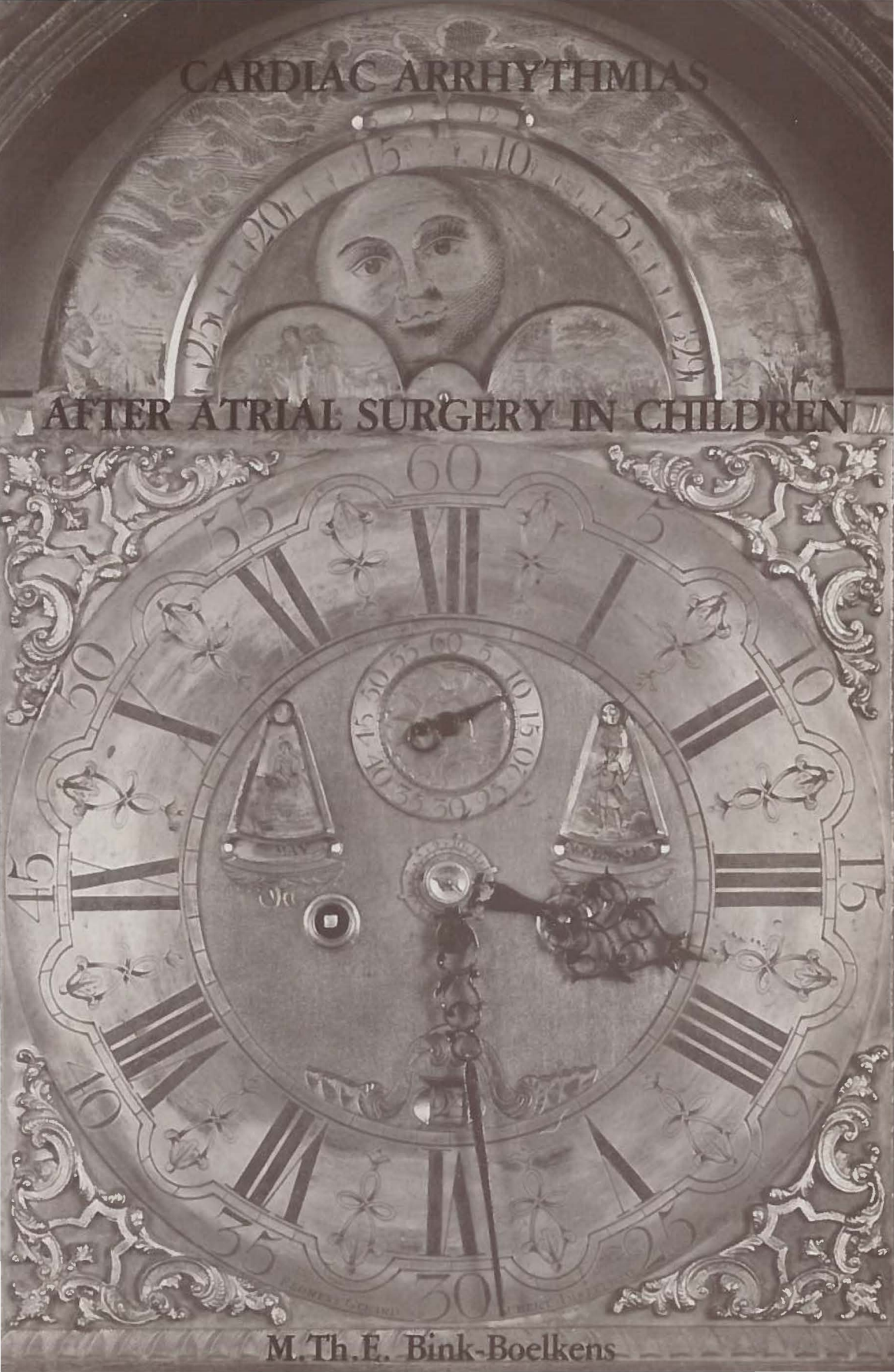
CARDIAC ARRHYTHMIAS AFTER ATRIAL SURGERY IN CHILDREN



M. Th. E. Bink-Boelkens

CARDIAC ARRHYTHMIAS
AFTER ATRIAL SURGERY IN CHILDREN

STELLINGEN

behorende bij het proefschrift

CARDIAC ARRHYTHMIAS AFTER ATRIAL SURGERY IN CHILDREN

door

Margaretha Theodora Elisabeth Boelkens

1. Inzicht in vóórkomen geeft uitzicht op voorkómen.

2. Een goede controle van patienten, die een Mustard operatie hebben ondergaan, moet naast de routine controle tenminste bestaan uit periodieke 24–uur E.C.G. analyse en colour coded Doppler echocardiografie.

3. Beschadiging van de sinusknoop tijdens een hartoperatie kan in belangrijke mate worden voorkomen door aanpassingen in de operatietechniek.

4. Het verdient de voorkeur kinderen met een boezemseptum defect te opereren tussen de leeftijd van één en drie jaar.

5. Een belangrijke voorwaarde om kinderen met een boezemseptum defect vroegtijdig te kunnen opereren, is een goede auscultatietraining voor consultatiebureau–artsen.

6. Bij het "sick sinus syndrome" na hartchirurgie is, net als bij het congenitale A.V.–block, niet de bradycardie maar de tachycardie levensbedreigend.

7. Achter het boezemfladderen na een hartoperatie gaat bij kinderen meestal een beschadigde sinusknoop schuil.

8. Indien supraventriculaire ritmestoornissen op de teenerleeftijd noodzaken tot jarenlange anti–aritmische medicatie, dan verdient ritmechirurgie de voorkeur.

9. Het is achterhaald een fixed–rate pacemaker te implanteren bij een kind met een bradycardie, gezien de huidige mogelijkheid tot rate–responsive en fysiologisch pacen.

10. Routinematig echocardiografisch screenen van de menselijke foetus leidt niet tot een significant betere levensverwachting van de pasgeborene.

11. De diagnose idiopathische gedilateerde cardiomyopathie mag op de kinderleeftijd alleen worden gesteld, als aangeboren afwijkingen van de kransvaten met behulp van angiografie zijn uitgesloten.

12. Wanneer een cytologische punctie uit een mammatumor nabloedt, is de kans op maligniteit groot.

13. Bij de besluitvorming over extremiteit–sparende chirurgie bij kinderen met een osteosarcoom dient men niet alleen rekening te houden met de te verwachten lengtegroei, maar ook met de toekomstige beroepskeuze en de individuele wensen voor sportbeoefening.

14. Het beoordelen van een klinische afdeling aan de hand van het aantal wetenschappelijke publicaties geeft vooral informatie over de wijze waarop de medewerkers hun (schaarse) vrije tijd besteden.

15. De meest voorkomende vorm van links–isomerisme (gespiegelde aanleg) is de aanwezigheid van twee linker handen.

16. Het zou veel geld besparen als in de academische ziekenhuizen de wachttijden voor patienten beperkt werden tot het "professoraal kwartiertje".

17. Het zal niet lang meer duren of het proefschrift wordt een floppy.

RIJKSUNIVERSITEIT GRONINGEN

CARDIAC ARRHYTHMIAS AFTER ATRIAL SURGERY IN CHILDREN

PROEFSCHRIFT

ter verkrijging van het doctoraat in de Geneeskunde
aan de Rijksuniversiteit Groningen
op gezag van de Rector Magnificus Dr. L.J. Engels
in het openbaar te verdedigen op woensdag 24 mei 1989
des namiddags te 2.45 uur precies

door

Margaretha Theodora Elisabeth Boelkens

geboren te Hengelo (O)

Promotores: Prof. Dr. J.R.G. Kuipers
Prof. P.C. Gillette M.D.

Promotiecommissie: Prof. Dr. A. Eygelaar
Prof. Dr. H.S.A. Heymans
Prof. Dr. H.J.J. Wellens

In dank aan mijn moeder en oom Henk

Voor en met Arnold

Paranimfen: Dr. H.P. Pull ter Gunne
Drs. A.J. Bink

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CONTENTS

VOORWOORD

Vrijwel ongemerkt is uit de poging een klinisch probleem op te lossen een serie artikelen ontstaan en zijn deze gebundeld in een proefschrift. Het onderzoek hiervoor werd verricht binnen de afdeling Kindercardiologie (Prof. Dr. J.R.G. Kuipers) van de kliniek voor Kindergeneeskunde (Prof. Dr. J. Fernandus, na 1987 Prof. Dr. H.S.A. Heymans). Gezien de aard van de problematiek was er een nauwe samenwerking met de afdelingen Thoraxchirurgie en Thoraxanaesthesie. Als eerste zou ik dan ook de collegae van deze drie afdelingen willen danken voor hun hulp, collegialiteit en vooral voor hun niet aflatend gevoel voor humor.

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Prof. Dr. Klaas K. Bossina maakte mij enthousiast voor de kindercardiologie en bereidde mijn stage in Houston voor, die zo belanrijk was voor het verdere verloop van mijn onderzoek.

Aan mijn opleiding in de kindergeneeskunde onder Prof. Dr. J.H.P. Jonxis bewaar ik zeer goede herinneringen.

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Dr. Martin L.J. Landsman en Arend Bergstra dank ik voor al het werk dat zij verrichtten bij het opstarten van de electrofysiologische catheterisaties in Groningen en voor hun hulp tijdens de vele catheterisaties die wij samen deden. Ook de verpleegkundigen, die mij in de loop der jaren tijdens de catheterisaties assisteerden, dank ik voor hun hulp en interesse.

De vele 24–uur E.C.G. recorders werden aangeplakt door Mevrouw Heleen M. Zuidema en Mevrouw Wil J. Poort. Ik ben dankbaar voor hun nauwgezetheid en voor de prettige sfeer, waarin wij konden werken. De medewerkers van de Stichting Fysiologic in Zeist analyseerden de 24–uur E.C.G.'s snel en met extra aandacht voor de specifieke problematiek; ook hen ben ik zeer erkentelijk.

Mevrouw Dr. Adri H. Cromme–Dijkhuis en Mevrouw Miek Schasfoort–van Leeuwen beoordeelden en maakten, respectievelijk, alle echocardiogrammen van de kinderen. Samen kregen wij daardoor een beter inzicht in de bijdrage van de echocardiografie aan de controle van de kinderen met de bestudeerde hartafwijkingen. Ik dank hen voor hun expertise en hulp.

Lodewijk Martijn verzorgde de tekeningen, Mevrouw Rita Klunder–van Bijssum verleende veel secretariële hulp, Paul Buchner verzamelde literatuur en Drs. F.G. Sluiter zorgde voor de "finishing touch" van het engels in de hoofdstukken Introduction, Discussion en Summary. Hiervoor allen mijn dank.

Tot slot dank ik Arnold voor al het "gereedschap", dat hij in de loop der jaren voor mij heeft gemaakt, in de vorm van computer programma's om mijn werk te vergemakkelijken en te versnellen. Ook de lay–out kwam van zijn "desk top". Vooral dank ik hem echter voor zijn begrip en stimulans ondanks het feit, dat er soms wel erg weinig vrije uurtjes overbleven.

CHAPTER 1

INTRODUCTION

INTRODUCTION

Since the first operation for congenital heart disease in 1938, cardiac surgery has developed rapidly. Today surgical correction or at least surgical palliation is possible for almost all types of congenital heart disease. This has resulted in a substantial improvement of the life expectancy and the quality of life of children with a congenital malformation of the heart.

One of the risks of cardiac surgery is that the conduction system of the heart, which is almost invisible for the surgeon, is damaged. The type of operation determines which part of the conduction tissue is at risk and which type of conduction abnormalities or arrhythmias can be expected postoperatively. Some of these conduction abnormalities are present immediately after operation, others develop during the years after operation. The explanation for the latter phenomenon is probably the progressive formation of scar tissue in and around the conduction tissue and the gradual degeneration of the cells of the conduction system. Not only damage to the conduction tissue itself can cause postoperative conduction abnormalities or arrhythmias, but also injury of the coronary artery branches that supply the oxygenated blood to the separate parts of the conduction system.

Much research is done by pathologists, among them Bharati and Lev [1] and Anderson, Ho, and Becker [2] to delineate the conduction system for the surgeon, in order to reduce the risk of damage of the conduction tissue during surgery. However, some congenital heart defects are so closely located to the conduction tissue and some surgical techniques make suturing so close to the conduction system necessary, that injury can not always be avoided.

We studied the arrhythmias seen after the Mustard operation for transposition of the great arteries and the surgical closure of atrial septal defects of the secundum type. Other surgical procedures are performed in the atrium for a variety of cardiac defects. However, the Mustard operation and the closure of an atrial septal defect accounted, until recently, for more than 60% of the surgical procedures performed in the atrium in childhood. Familiarity with the anatomy of the conduction system and the surgical technique of the Mustard operation and the closure of an atrial septal defect is necessary to understand why the conduction system may be injured by these operations.

Anatomy of the conduction system in the atrium (Fig. 1).

In normal conditions the sinus node provides the impulse formation, under the influence of the autonomic nervous system. The electrical impulse is propagated by the atrial myocardium to the atrioventricular node. After lengthy discussions, pathologists [1,2] at last decided that the internodal conduction was not effected by specialized conduction tissue, but by normal

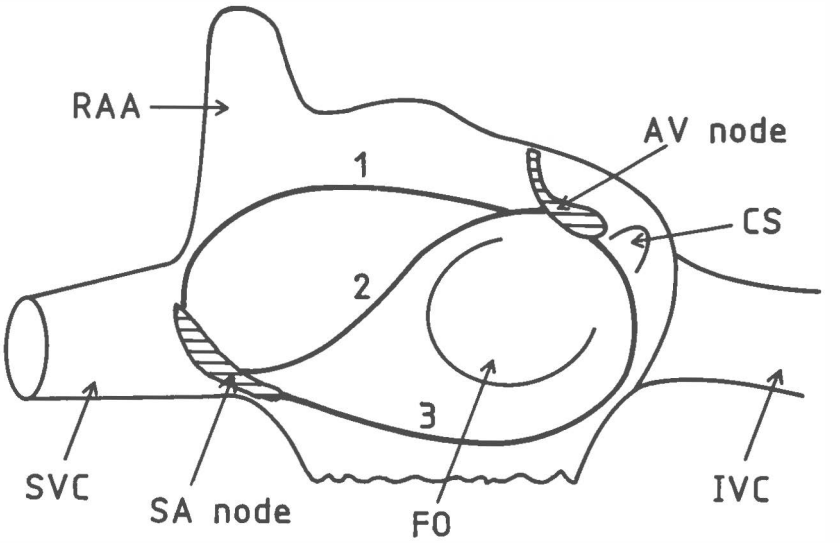

Fig. 1. The position of the conduction system in the right atrium (as seen by the surgeon).
CS = coronary sinus; FO = fossa ovalis; IVC = inferior vena cava; RAA = right atrial appendage; SVC = superior vena cava; 1,2,3 = superior, middle, and inferior preferential pathway respectively.

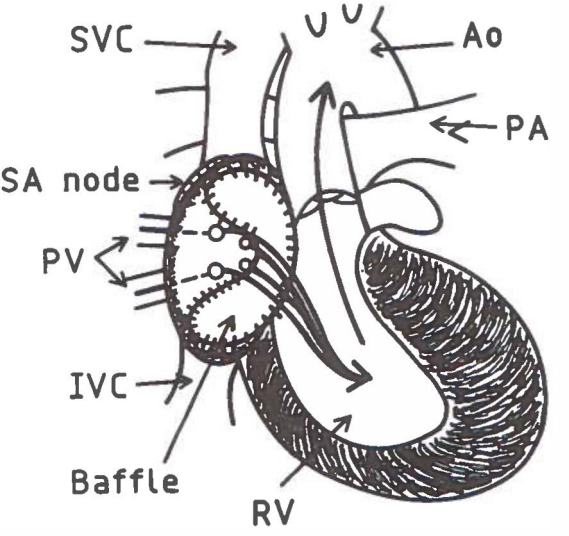

Fig. 2. The Mustard operation for transposition of the great arteries.
Ao = aorta; IVC = inferior vena cava; PA = pulmonary artery; PV = pulmonary vein; RV = right ventricle; SVC = superior vena cava.

atrial myocardium. However, there are preferential pathways of thicker atrial muscle bundles, but their pattern can be accounted for simply by the geometric arrangement of the muscle bundles in the right atrium. When the atrial contraction is finished, the atrioventricular node conducts the electrical impulse through the bundle of His, and the bundle branches to the ventricular myocardium.

The sinus node is a subepicardial cigar–shaped structure, located in the terminal groove extending to the junction of the right atrial appendage and the superior vena cava. The superior and middle preferential pathways originate from the sinus node, superior and inferior to the superior vena cava and follow the limbus of the fossa ovalis to the atrioventricular node. The inferior preferential pathway follows the sulcus terminalis, distal to the coronary sinus, to the atrioventricular node. The atrioventricular node is located in the triangle of Koch, between the septal leaflet of the tricuspid valve and the coronary sinus.

Blood supply to the sinus node is through a proximal branch of the right (55%) or the left (45%) coronary artery. The artery runs either clockwise or counterclockwise around the superior vena cava, and sometimes even forms a circle around the superior vena cava. Blood supply to the atrioventricular node is through a terminal branch of the right coronary artery (90%).

Transposition of the great arteries.

The main abnormality of the heart with transposition of the great arteries is a discordant ventriculo–arterial connection. The result of this is a parallel circulation, in which the low–saturated systemic venous blood is directed from the right ventricle to the aorta instead of to the pulmonary artery, and the high–saturated blood is directed from the left ventricle to the pulmonary artery instead of to the aorta.

MUSTARD OPERATION (PHYSIOLOGIC CORRECTION) (Fig. 2).

In 1964 Mustard [3] developed a surgical technique for physiological correction of this anomaly. Instead of switching the arterial outflow of the heart (which was unsuccessful until recently), he redirected the venous inflow. The systemic venous flow was redirected to the left ventricle and the pulmonary artery by a pericardial or prosthetic tunnel ("baffle") in the atria. The pulmonary venous flow was redirected at atrial level to the right ventricle and the aorta.

The risk for the conduction system is considerable. The baffle is sutured very close to the sinus node, and enlargement of the intra–atrial communication can result in interruption of at least the inferior preferential pathway. A cutdown of the coronary sinus in order to create a normal drainage to the

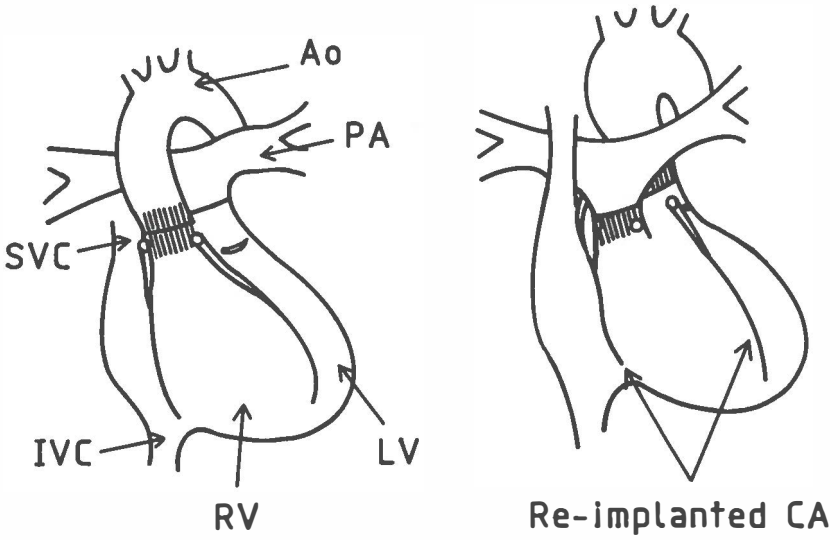

Fig. 3. The arterial switch operation for transposition of the great arteries.
Ao = aorta; CA = coronary arteries; IVC = inferior vena cava; LV = left ventricle; PA = pulmonary artery; RV = right ventricle; SVC = superior vena cava.

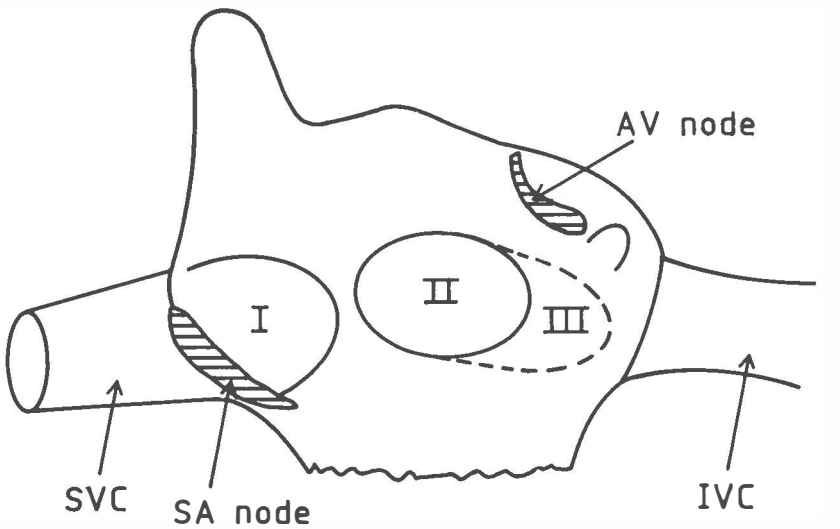

Fig. 4. Atrial septal defects (as seen by the surgeon).
I = sinus venosus type atrial septal defect; II = fossa ovalis type atrial septal defect (ostium secundum defect); III = fossa ovalis type, extending to the inferior vena cava; IVC = inferior vena cava; SVC = superior vena cava.

systemic atrium can damage the atrioventricular node; this also applies to the sutures of the baffle close to the atrioventricular node.

Senning [4] described and performed a comparable operation a few years before Mustard, but he used the atrial wall instead of prosthetic material to create the physiologic correction. We have no experience with this operation.

ANATOMIC CORRECTION OF TRANSPOSITION OF THE GREAT ARTERIES (ARTERIAL SWITCH OPERATION) (Fig. 3).

In 1975 Jatene [5] published a preliminary report of the first successful anatomical correction of transposition of the great arteries. The operative mortality was very high at first; only in recent years has the operative mortality decreased rapidly. We will discuss this arterial switch operation in Chapters 4 and 7. The technique of this operation consists of transsecting the great arteries and connecting the proximal aorta to the distal pulmonary artery and vice versa. The coronary arteries are taken out of the proximal aorta (future pulmonary artery) with a cuff of surrounding vessel wall and are implanted in the proximal pulmonary artery (future aorta). The difficulty and the risk of this operation are formed by the transplantation of the coronary arteries and the necessity to perform this operation in the first 1–2 weeks after birth, before the left ventricular wall becomes too thin to maintain the systemic circulation.

Atrial septal defect (Fig. 4).

The fossa ovalis type atrial septal defect is the most common type of atrial septal defect. It is located in the middle of the septum, caused by a perforation, deficiency or absence of the valve of the foramen ovale.

The sinus venosus defect is located in the atrial septum adjacent to the orifice of the superior vena cava, and is mostly accompanied by a partial abnormal drainage of the pulmonary veins. Rarely is this type of defect located at the entrance of the inferior vena cava.

Atrial septal defects can be closed directly or by a patch. Abnormal draining pulmonary veins are diverted to the left atrium by the same patch that closes the atrial septal defect.

In the fossa ovalis type defect, the atrioventricular node and at least the superior and middle preferential pathways are at risk of being damaged. In the sinus venosus type of atrial septal defect, the patch has to be sutured in the close vicinity of the sinus node and the sinus node artery.

Clinical consequences of injury of the conduction system.

Sinus node: Dysfunction of the sinus node can lead to a variety of arrhythmias. Primarily a depressed automaticity causes bradycardia with an insufficient

response of the heart rate to exercise. The impulse formation can still originate in the sinus node (sinus–bradycardia, sinus–arrest), but is often taken over by subsidiary atrial or atrioventricular junctional escape foci. Bradycardia provokes tachy–arrhythmias, therefore, sinus node dysfunction often presents as a brady–tachy syndrome. Bradycardia is accompanied by premature beats, attacks of supraventricular tachycardia, atrial flutter or atrial fibrillation.

Atrium: As described above, the preferential internodal pathways are the main routes of conduction between the sinus node and the atrioventricular node. However, even after a complete intersection of all these preferential pathways there still is conduction through the remaining atrial myocardium to the atrioventricular node [6]. This conduction will be slower than normal. Areas of slow conduction facilitate the development of reentrant tachycardias including atrial flutter.

Atrioventricular node: Damage to the atrioventricular node results in atrioventricular conduction disturbances, such as first, second and third–degree atrioventricular block, and seldom in enhanced automaticity of the atrioventricular node.

Objectives and design of this thesis.

The studies described in this thesis originate from a clinical problem. We successfully performed the Mustard operation for transposition of the great arteries in our hospital. The operative mortality was very low, most children being able to lead an almost normal life. However, several children developed arrhythmias that had to be treated with anti–arrhythmic drugs or pacemaker implantation. Some children died suddenly many years after an apparently successful operation.

Closure of an atrial septal defect is a "simple" operation with a mortality approaching 0%. The life expectancy and the quality of life for these children after operation should be equal to children with normal hearts. Nevertheless, some children developed arrhythmias comparable with those seen after the Mustard operation, and some needed drug treatment or pacemaker implantation.

The objectives of the studies described in this thesis are:

— to analyze the incidence and the severity of arrhythmias after the Mustard operation and after surgery for atrial septal defect.
— to study the natural history of these arrhythmias.
— to detect possible correlations with the surgical technique.
— to judge the effect of surgical modifications for prevention of postoperative arrhythmias.

— to investigate the role of possible preoperative electrophysiologic abnormalities and arrhythmias in patients with an atrial septal defect.

The studies referring to the arrhythmias after the Mustard operation for transposition of the great arteries are described in Chapters 2, 3, and 4. The studies relating to the arrhythmias after surgical closure of an atrial septal defect are described in Chapters 2, 5, and 6. Chapter 7 consists of a general discussion and our final conclusions.

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CHAPTER 2

DYSRHYTHMIAS AFTER ATRIAL SURGERY IN CHILDREN

American Heart Journal 1983;106:125–130

DYSRHYTHMIAS AFTER ATRIAL SURGERY IN CHILDREN

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SUMMARY

A retrospective study was done in 50 patients after Mustard's operation (group A) and in 204 patients after closure of a secundum atrial septal defect (group B) to analyze the postoperative dysrhythmias and to relate them to surgical factors. Forty–two percent of the patients in group A had dysrhythmias at the end of the follow–up, compared to 23% of group B patients. There was a high late mortality in group A (16%) significantly related to atrial flutter and atrioventricular junctional rhythm. In group A a significant correlation was found between dysrhythmias and age at operation, use of cardioplegia, perfusion time, and the type of cannulation. In group B there was a significant relation between the location of the defect and the presence of abnormal pulmonary venous drainage. After ASD closure using hypothermia instead of cardiopulmonary bypass, the incidence of dysrhythmias was significant lower. Damage to the sinus node by cannulation and by suturing in the sinus node area is the main cause of the high incidence of dysrhythmias after atrial surgery. This high incidence should be a factor in the consideration of new types of operations.

INTRODUCTION

Shortly after the first description of the Mustard correction for transposition of the great arteries [1], several authors [2–4] reported early and late dysrhythmias and sudden death after the procedure. Later a decrease in dysrhythmias after a change in surgical technique, especially with regard to cannulation and suturing of the baffle, was reported [5,6]. However, a considerable percentage of postoperative Mustard patients still have dysrhythmias. There is an indication that the incidence of dysrhythmias increases during the follow–up period [7,8]. Fewer reports are available [9,10] about the closure of atrial septal defect (ASD). It is well known that people with an unoperated ASD tend to develop dysrhythmias at a later age [11]. Postoperatively the same type of dysrhythmias as after the Mustard operation has been described, but with a lower incidence.

Surgical damage to the sinus node, the sinus node artery [5,12], or to the main connections between the sinus– and the AV node has been suggested as the cause of these dysrhythmias [13,14]. There is pathologic [4,15] and electrophysiologic [16–18] evidence of damage to the sinus node. The role of atrial conduction is still dubious [16,17]. The aim of our study was to quantify and to qualify the dysrhythmias after Mustard operation and ASD closure, and to learn the natural history of the dysrhythmias, their correlations with the surgical procedure and, if possible, ways to prevent these rhythm disturbances. The study was also done in view of the possibility of other operations for transposition of the great arteries, as described by Senning and Jatene [27].

METHODOLOGY

Between 1969 and 1980 a Mustard operation was performed in 61 patients with transposition of the great arteries. In 17 patients a ventricular septal defect (VSD) closure was performed at the same time. The 50 survivors formed *group A*. Patients with a palliative Mustard procedure were included in the study. The period 1969 to 1980 was chosen to estimate the effect of a change in cannulation technique established in 1977. *Group B* included 204 patients operated for a secundum type ASD between 1967 and 1980. Patients with partial or total anomalous pulmonary venous return were included. Patients with associated anomalies, requiring a ventriculotomy, were excluded from the study. In the first 3 years, ASD closure was performed using hypothermia. Later cardiopulmonary bypass was used. This enabled us to judge the effect of cannulation on the incidence of dysrhythmias. All the transposition

Table I. Incidence of dysrhythmias after Mustard operation (group A)

Preoperatively	8%
At least once in follow-up	64%
6 to 8 weeks postoperatively	40%
At the end of follow-up	42%

patients and nearly all the ASD patients had their entire follow–up in our department. Each child was operated in the Department of Thoracic Surgery of the University of Groningen. Data from the preoperative period, the operation, and the postoperative period were collected. All the pre– and postoperative ECGs were analyzed for dysrhythmias. Although there were individual differences in the number of ECGs taken per year, the general tendency for group A was preoperatively twice a year and postoperatively twice to once a year. In group B in general an ECG was taken once a year in the pre– and postoperative periods. Holter recordings and exercise tests were performed. These data were not included in the study, because there were no preoperative Holter or exercise studies done. Data analysis was performed with the Statistical Package for Social Studies, using the χ^2 test.

GROUP A (MUSTARD OPERATION)

Study patients.

There were 50 patients surviving after Mustard operation. Their ages at operation ranged from 1 month to 19.7 years (mean 3.2 years). The follow–up period was 3 months to 8.5 years (mean 3.1 years). A standard Mustard operation was performed, using Dacron material in the majority of patients. Before 1977 the superior vena cava (SVC) was cannulated through the right atrial appendage. Since 1977 the cannulation was performed in the upper part of the SVC.

Incidence of dysrhythmias (Table I).

Eight percent of the patients had dysrhythmias in the preoperative period. Sixty–four percent had dysrhythmias at least once during the postoperative and follow–up periods. Twenty–eight percent had severe dysrhythmias, e.g., atrial fluter, or bradycardia or brady–tachy syndrome. In two patients pacemaker implantation was necessary. The dysrhythmias were not stable. They disappeared and reappeared in the same patient during the follow–up period. Fifty percent of the dysrhythmias developed after discharge from the hospital. About 6 to 8 weeks after surgery 40% of the patients had dysrhythmias.

Table II. Type of dysrhythmias after Mustard operation (group A)

Sinus node dysfunction	50%
AV junctional rhythm	31%
Atrial flutter	25%
Premature atrial contractions	25%
Premature ventricular contractions	22%

Table III. Late mortality and dysrhythmias (group A)

Mean late mortality 8 patients (50)	16%
Late mortality in patients with SND	19%
Late mortality in patients with AVJ	40% $p < 0.02$
Late mortality in patients with AF	62% $p < 0.0001$

AVJ = AV junctional rhythm; AF = atrial flutter; SND = sinus node dysfunction.

This percentage remained nearly the same during the whole follow–up period. If the ECG was (ab)normal 6 to 8 weeks postoperatively, it remained (ab)normal during the follow–up period in 70% of the cases.

Type of dysrhythmias (Table II).

The majority of the children had more than one type of dysrhythmia. Fifty percent of the patients with dysrhythmias showed sinus node dysfunction (SND) defined as sinus bradycardia, sinus arrest, or sinoatrial exit block. Thirty–one percent had an AV junctional rhythm (AVJ) and 25% had atrial flutter (AF). Besides this, 25% had premature atrial contractions (PACs) and 22% had premature ventricular contractions (PVCs). There was a strong correlation between the different types of rhythm. Fig. 1 shows that 50% of patients with AF in one ECG had AVJ in another ECG. Forty percent of patients with AVJ also had AF in follow–up. The same applied to AVJ and SND, and AF and SND. None of the patients showed AV conduction disturbances.

Late mortality (Table III).

There was a high late mortality in group A. Eight patients (16%) died suddenly. In six of these patients dysrhythmias were the cause of death. The period between the operation and sudden death was 0.3 to 5.4 years (mean 1.8 years). These children did not differ from the whole group in relation to age

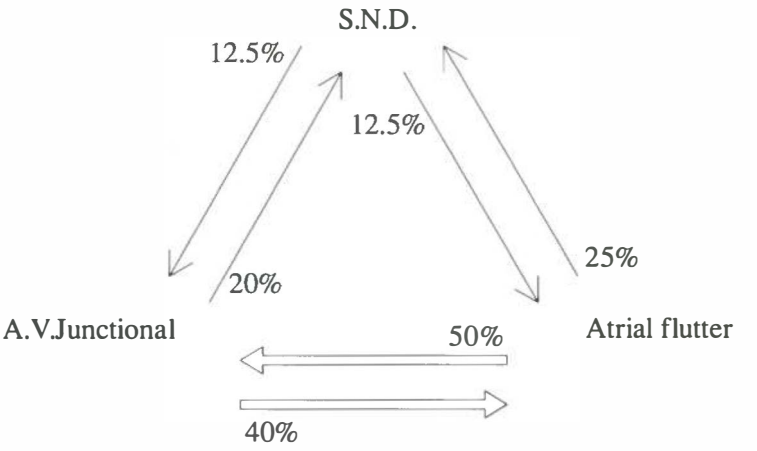

Fig. 1. Correlation between the different types of dysrhythmias after Mustard operation (group A).
AV = atrioventricular; SND = sinus node dysfunction.

Table IV. Correlation with dysrhythmias (group A)

Nonsignificant	Significant
Sex	Age at operation $p < 0.009$
Associated anomalies	Use of cardioplegia $p < 0.004$
Ischemic time	Perfusion time Type of cannulation $p < 0.008$

at operation, associated anomalies, and year of operation. There was a very significant relation between the type of dysrhythmias and the occurence of sudden death. The late mortality in patients with SND was 19%, with AVJ it was 40% ($p < 0.02$), and with AF it was 62% ($p < 0.0001$).

Correlations with dysrhythmias (Table IV).

There were no correlations between dysrhythmias and sex, associated anomalies (VSD), or ischemic time during operation. On the other hand, there were significant correlations with age at operation, use of cardioplegia, time of perfusion, and type of cannulation. The incidence of dysrhythmias increased with the age at operation ($p < 0.009$). The older patients mainly underwent palliative Mustard operations because of pulmonary hypertension. The percentage of dysrhythmias decreased significantly after the introduction

Table V. Type of ASD and operation method (group B)

Type of ASD		Operation method	
Fossa ovalis type	78%	Direct closure	40%
Sinus venosus type	10%	Patch closure	60%
IVC type	12%	Hypothermia	22%
		Cardiopulmonary bypass	78%

ASD = atrial septal defect; IVC = inferior vena cava.

Table VI. Incidence of dysrhythmias after ASD closure (group B)

Preoperatively	2%
At least once in follow-up	35%
6 to 8 weeks postoperatively	23%
At the end of follow-up	23%

Table VII. Type of dysrhythmias after ASD closure (group B)

AV junctional rhythm	46%
Sinus node dysfunction	39%
Atrial flutter	18%
Premature atrial contractions	35%
Premature ventricular contractions	25%

of cardioplegia ($p < 0.004$). With a perfusion time of less than 70 minutes, no child developed dysrhythmias, and with a perfusion time longer than 150 minutes 100% developed these rhythm disturbances. When the SVC cannulation was performed through the right atrial appendage, 77% had dysrhythmias at least once during the follow–up; with cannulation high in the SVC, only 33% developed dysrhythmias at least once ($p < 0.008$).

GROUP B (ATRIAL SEPTAL DEFECT TYPE II)

Study patients.

There were 204 patients after closure of an ASD. Age at operation was 0.1 to 17.2 years (mean 7.5 years). The period of follow–up was 0.1 to 8.2 years (mean 2.3 years). Seventy–eight percent of the ASDs were of the fossa ovalis type, 10% were located near the SVC (sinus venosus type), and 12% were located near the IVC (IVC type) (Table V). Twenty–two percent of the patients had partial anomalous pulmonary venous drainage. In 22% the operation was

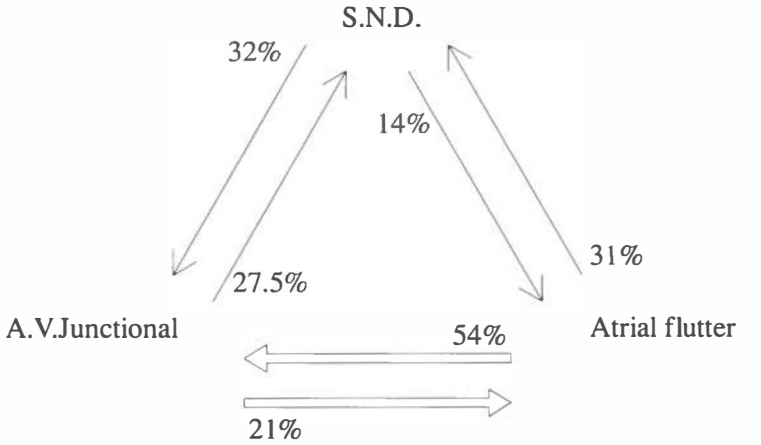

Fig. 2. Correlation between the different types of dysrhythmias after ASD closure (group B).
AV = atrioventricular; SND = sinus node dysfunction.

performed without cannulation, using hypothermia. The remaining 78% were operated using cardiopulmonary bypass. Cannulation of the SVC was performed through the right atrial appendage. Forty percent of the ASDs were closed directly; in 60% the ASD was closed by a patch. In 17% a valvotomy of the pulmonic valve was performed through the pulmonary artery.

Incidence of dysrhythmias (Table VI).

Two percent of the children showed dysrhythmias in their preoperative ECGs, and 35% had dysrhythmias at least once during the postoperative follow–up periods. Ten percent of group B had severe dysrhythmias. In four patients a pacemaker implantation was necessary for treatment of a bradycardia or a brady–tachy syndrome. Fifty–six percent of the dysrhythmias developed after discharge from the hospital. Six to 8 weeks postoperatively 23% of the patients had dysrhythmias and also 23% had dysrhythmias at the end of the follow–up period. A normal ECG at 6 to 8 weeks postoperatively was more predictive than in group A; 90% still had a normal ECG at the end of the follow–up period.

Type of dysrhythmias (Table VII).

As in group A, most of the children had more than one type of dysrhythmia. AVJ was the most common type (46%); SND was seen in 39% and AF in 18%. Besides this, 35% had PACs and 25% had PVCs. Fig. 2 shows the same correlation between the three types of dysrhythmias as was seen in group A.

Table VIII. Correlations with dysrhythmias (group B)

Nonsignificant	Significant
Sex	Type of ASD $p < 0.03$
Age at operation	Abnormal pulmonary venous return $p < 0.03$
Ischemic time	Hypothermia or c.p. bypass $p < 0.008$
Perfusion time	
Cardioplegia	
Patch or direct closure	

ASD = atrial septal defect; c.p. bypass = cardiopulmonary bypass.

Late mortality.

There was no late mortality in the group of patients after ASD closure.

Correlations with dysrhythmias (Table VIII).

As in group A, there were no significant correlations with sex and ischemic time during operation. Other than in the transposition group, there were no correlations with age at operation, cardioplegia, and perfusion time. There also was no significant difference in the incidence of dysrhythmias, whether the ASD was directly closed or closed by a patch. There were significant correlations between the incidence of dysrhythmias and the type of ASD, the presence of abnormal pulmonary venous return, and with the use of cannulation. The incidence of dysrhythmias was significantly lower if the ASD was located near the inferior vena cava (IVC) ($p < 0.03$). In the patients with abnormal pulmonary venous return, the incidence was significantly higher ($p < 0.03$). The most significant correlation was found with regard to the cannulation. All the patients operated with hypothermia had a fossa ovalis type defect, which was directly closed. We compared these patients with the same group operated on by cardiopulmonary bypass. In the former group 11% had dysrhythmias at least once during the follow-up period; in the latter group 50% had these rhythm aberrations ($p < 0.008$).

COMMENTS

Incidence and type of dysrhythmias.

We found a considerable frequency of dysrhythmias in the patients after a Mustard operation (42% of patients). This percentage, however, is comparable to data from other centers [5,19], except for the low incidence

reported by Southall et al. [20] and by Oelert et al. [21]. In 28% of the patients the dysrhythmias were severe, making antidysrhythmic medication or pacemaker implantation necessary in children with otherwise good operation results.

The incidence of dysrhythmias in the postoperative ASD patients was less (23%), but 10% still had severe dysrhythmias after operation for this relatively "simple" congenital heart defect. Preoperatively there was only a low percentage of dysrhythmias and no indication for antidysrhythmic drugs. It is well known that patients with an unoperated ASD tend to develop dysrhythmias at an older age. One is tempted to ask if ASD closure does not create as many dysrhythmias as it prevents [22]. The number of dysrhythmias found, depends partly on the number of ECGs taken. We think that the number of ECGs taken in both groups was not abnormally high, and it is therefore not likely that this factor explains the high incidence of dysrhythmias. With some exceptions, the number of pre– and postoperative ECGs in the individual patient was comparable, justifying comparison of the pre– and postoperative dysrhythmias.

The type of dysrhythmias was the same in both groups. They were all supraventricular in origin – decreased sinus node automaticity, AVJ escape rhythm, or atrial flutter. No AV conduction disturbances or ventricular dysrhythmias were seen, except for isolated PVCs. The dysrhythmias in both groups developed in 50 to 60% post discharge. The percentage in the whole group stabilized 6 to 8 weeks postoperatively. In the individual patient there still was a considerable variation in rhythm after this period. Wittig et al. [17] suggested that there possibly were two different mechanisms in creating SND and AF on the one hand and AVJ on the other. From our data it seems more likely that in Mustard and ASD patients one condition causes the combination of dysrhythmias with the same course at follow–up. The only argument against it, is the difference in the percentage of sudden death between SND and AVJ or AF.

Late mortality.

There was a very high late mortality in group A, higher than the 4% known from the literature [19,20,23]. Sudden death occured even 5.4 years postoperatively. An important finding is the significant relation between sudden death and AF and / or AVJ. It is likely that death results from a long pause at the transition of AF to an escape rhythm. The other possibility is that ventricular fibrillation, due to a fast response to AF, is the cause of death. In fact, two of our patients died with a well–functioning pacemaker. One died at home and the other showed ventricular fibrillation on arrival at the hospital. It is understandable that a child with transposition of the great arteries, who

had a mean period of cyanosis of 3 years, would tolerate the dysrhythmias less than an ASD patient. In this group there was no sudden death till the end of the study. Later, however, one patient died suddenly, and again this patient had AF.

Correlations.

In group A there was a significant correlation with perfusion time. There are two ways to explain this, either by the negative effect of a prolonged perfusion on the myocardium or by a prolonged period of cannulation and pressure on the sinus node area. The significant decrease in dysrhythmias since the use of cardioplegia, points in the former direction; the significant relation between dysrhythmias and the type of cannulation points in the latter. In groups A and B cannulation seems to be an important factor in creating dysrhythmias. Cannulation performed high in the SVC decreased the incidence. Operation of an ASD without cannulation gave an even more striking decrease compared to operation with cardiopulmonary bypass. These findings agree with the results of Clarkson et al. [24] in operations with one atrial cannula. As was suggested by others [17], suturing in the area of the sinus node is also of importance. Because of the retrospective character of the study, we could not find data concerning this theory in transpositions. The finding in group B, however, that the lowest incidence of dysrhythmias was seen in the IVC type of ASD, far away from the sinus node and the highest in abnormal pulmonary venous return (RA–SVC junction), supports this theory. It is likely that suturing is an added factor to the damage done by the cannulation, typical for atrial surgery. From our data it was not possible to judge the effect of the atriotomy. Without electrophysiological studies, it is also impossible to evaluate the role of slowed atrial conduction. The incidence of AF in our group is high. AF is facilitated by delayed atrial conduction [25]. Thus slowed conduction may be a third additional factor in creating dysrhythmias after atrial surgery.

CONCLUSIONS

The high incidence of dysrhythmias after atrial surgery seems to be the result of the cannulation and suturing in the area of the sinus node. Delayed atrial conduction is possibly a third factor, facilitating AF. The population at risk of sudden death is the group of children with atrial flutter and / or AVJ rhythm. The natural history and the types of dysrhythmias are the same for postoperative Mustard and ASD patients. The severity differs, possibly depending on the condition of the myocardium.

Concerning the prevention of damage to the sinus node, the technique described by Hariman et al. [26] of recording the sinus node ECG during the operation might be of help. If the incidence of dysrhythmias stays high despite further surgical modifications, one should consider other types of operations – e.g., the arterial switch operation described by Jatene et al. [27] for transpositions, or the ASD closure by catheter as described by Rashkind [28]. In the treatment of dysrhythmias after atrial surgery, the patients with AF and AVJ are at risk of sudden death. This knowledge justifies vigorous treatment with potential pacemaker implantation and antidysrhythmic drugs.

Acknowledgements.

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CHAPTER 3

LONG–TERM FOLLOW–UP OF DYSRHYTHMIAS FOLLOWING THE MUSTARD PROCEDURE

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LONG–TERM FOLLOW–UP OF DYSRHYTHMIAS FOLLOWING THE MUSTARD PROCEDURE

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SUMMARY

Earlier reports have suggested that the incidence of dysrhythmias after the Mustard procedure can be reduced if the sinoatrial node (SAN) is protected during surgery. To determine if these initial differences continue after longer follow–up, we examined all ECGs available for three groups of patients operated upon from January, 1965, through December, 1977. Group A included 37 patients who survived the operation prior to January, 1972, when surgical modifications were initiated to protect the SAN; group B included 44 patients available for follow–up who were operated upon from 1972 through 1974; and group C consisted of the 39 patients available for follow–up operated upon from 1975 to 1977. Dysrhythmias were classified as passive (failure of initiation or propagation of the SAN impulse), active (atrial flutter or supraventricular tachycardia), or atrioventricular (AV) conduction defects. Results were expressed as the incidence per number of different rhythms during follow–up intervals. The incidence of sinus rhythm in groups B and C (80%) was much greater than in group A (27%) during the first 2 years. However, after 8 years, less than 50% of the rhythms were sinus. Both brady– and tachydysrhythmias were common. Seven patients (6%) required pacemaker insertion for symptomatic sick sinus syndrome. Therefore despite efforts to protect the sinus node, late occurring dysrhythmias remain a significant problem in the postoperative Mustard patient.

INTRODUCTION

A serious long–term complication following the Mustard operation for transposition of the great arteries is the brady–tachydysrhythmia syndrome [1–4]. It resembles the sick sinus syndrome seen in adults. In 1974, we reported a high incidence of the syndrome following the classical Mustard procedure, but a lower incidence when the sinus node was protected by high superior vena cava cannulation and careful baffle insertion [5]. The purpose of this study was to determine if these initial improvements continue after longer follow–up.

METHODS

Patients.

In the 13–year period from January, 1965, through December, 1977, Mustard's technique of intra–atrial baffle repair of transposition of the great arteries was performed in 256 patients at the Texas Children's Hospital in Houston, Texas. Ninety–six patients were operated upon prior to January, 1972, when the changes in surgical technique were instituted. Eighty–three patients were operated upon between 1972 and 1974, and 77 patients between 1975 and 1977 (Table I). Group A consisted of the 37 patients in the initial group who were available for follow–up from 6 weeks to 14 years later. Those patients operated upon after efforts were made to minimize sinoatrial node (SAN) damage and available for follow–up comprised Groups B (44 patients) and C (39 patients). They were followed from 6 weeks to 9 years. Groups A and B are the same as in our 1974 report. Group C is a new group operated on since 1974.

Dysrhythmia types.

Three types of dysrhythmia were observed postoperatively. Those due to failure of initiation or propagation of the sinus impulse were designated passive dysrhythmias. These included marked sinus bradycardia with junctional escape, slow atrial rhythms, and slow junctional rhythms. The second type was characterized by rapid atrial or atrioventricular (AV) junctional impulses. These were termed active dysrhythmias and included supraventricular tachycardia and atrial flutter. AV conduction disturbances comprised the third type. Because many children from foreign countries have surgery in our institution, it is not possible to obtain follow–up on each of them. We feel that the lack of follow–up is random and due to geography. It is possible that the incidence of dysrhythmias is overestimated because symptomatic patients are more likely

Table I. Patient population

	1965–1971 Group A	1972–1974 Group B	1975–1977 Group C
No. of operations	96	83	77
No. of survivors	70	67	68
Follow–up patients	37	44	39
Length of follow–up	6 wk–14 yr	6 wk–9 yr	6 wk–6 yr
Mean	8.9 yr	4.7 yr	2.8 yr

Table II. Longitudinal dysrhythmia data

	6 wk–1 yr	1–2 yr	3–4 yr	5–7 yr	8–11 yr	12–16 yr
Group A						
No. rhythms	45	37	38	20	23	12
No. patients	37	28	28	18	20	10
Group B						
No. rhythms	38	52	30	31	11	–
No. patients	33	39	26	27	10	–
Group C						
No. rhythms	43	38	31	20	–	–
No. patients	39	33	29	17	–	–

to return, but this may be balanced by patients who die without our being aware.

Longitudinal evaluation.

All resting ECGs in the three patient groups were reviewed and classified as either sinus rhythm or one of the dysrhythmia types. Quite frequently, a single patient would have several different rhythms during a follow–up interval. Therefore, the results were expressed as the incidence per number of different rhythms during the study intervals. Table II lists the number of patients and rhythms during each follow–up period.

RESULTS

Sinus rhythm.

The incidence of sinus rhythm in groups B (81%) and C (79%) was greater than in group A (29%) during the initial postoperative years. However, 5 to 8

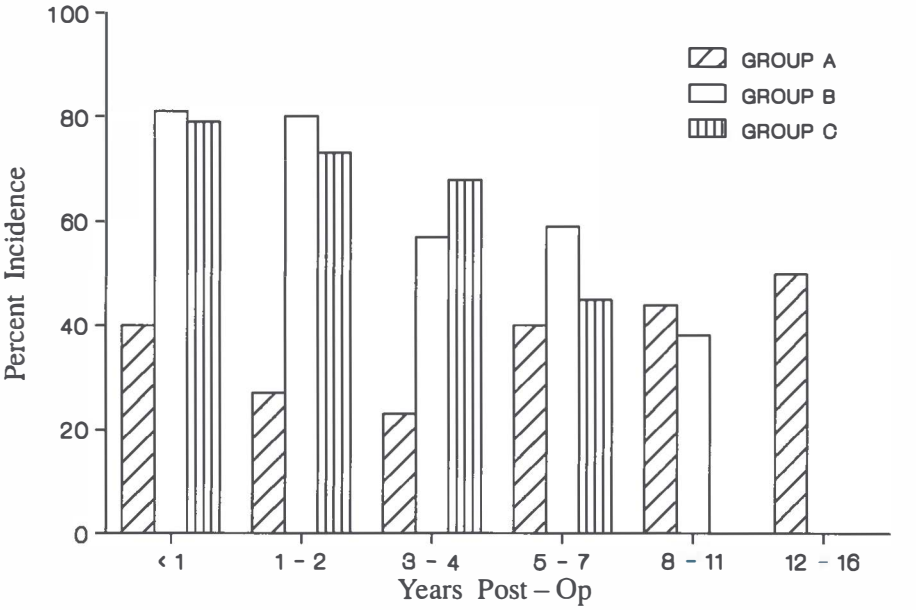

Fig. 1. Percent incidence of sinus rhythm after the Mustard operation.

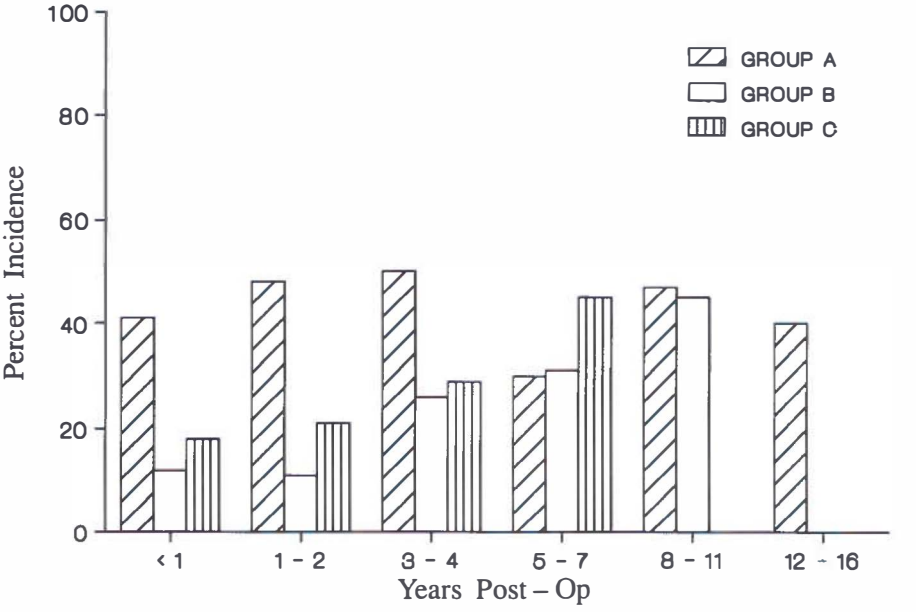

Fig. 2. Percent incidence of passive and paced rhythms after the Mustard operation.

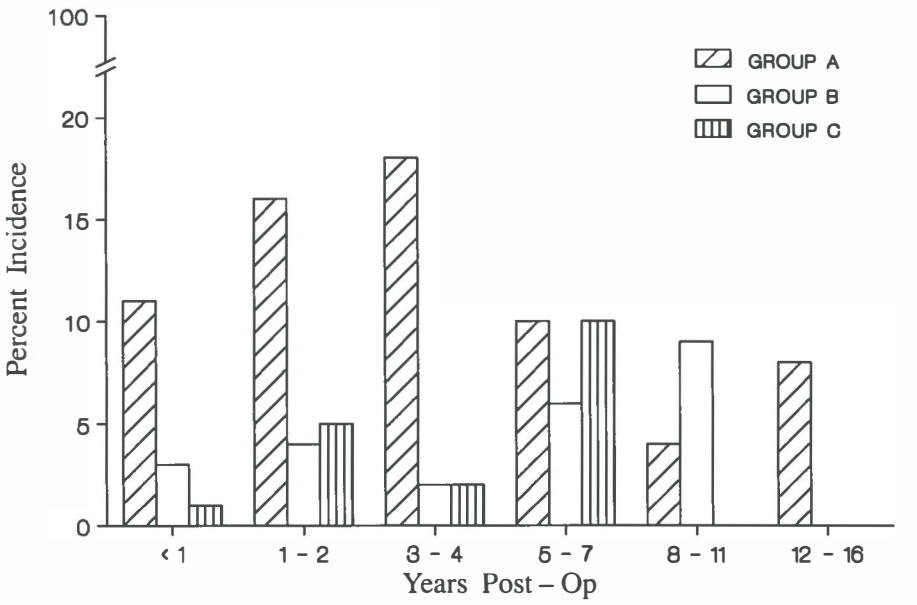

Fig. 3. Percent incidence of active dysrhythmias after the Mustard operation.

years later, the difference is much less (40%, 50%, and 45% for groups A, B, and C, respectively) (Fig. 1).

Passive dysrhythmias.

Coincident with the late decrease in sinus rhythm, there is a relative increase in the frequency of late occuring passive dysrhythmias in groups B and C. During the 8– to 11–year intervals, 45 to 47% of the rhythms were either paced or of the passive type (Fig. 2).

Active dysrhythmias.

The overall incidence of active dysrhythmias were greatest in group A, but remained less than 20% for each of the three groups (Fig. 3).

AV conductive disturbances.

AV conduction disturbances were limited to first–degree AV block. The incidence varied between 4 to 20% in the three groups. Many patients were receiving digitalis, which might account for the finding.

Table III. Pacemaker insertion in Mustard patients

	Years post–op	Mean
Group A (2/70 patients)	11,12	11.5 yr
Group B (3/67 patients)	7,5,5	5.6 yr
Group C (2/68 patients)	2,1	1.5 yr

Pacemaker insertion.

Two of the 70 survivors from group A ultimately required pacemakers for symptomatic sick sinus syndrome. Three of the 67 survivors from group B and two from group C required pacemakers for symptomatic bradycardia. The mean time from operation to pacemaker insertion was 11.5 years in group A, 5.6 years in group B, and 1.5 years in group C (Table III). The earlier insertion of pacemakers in the latter two groups probably reflects a greater acceptance of pacemaker therapy in children as a therapeutic modality rather than a difference among the three groups.

DISCUSSION

Pathologic and electrophysiologic studies have implicated damage to the sinus node as the most likely cause of dysrhythmias in the postoperative Mustard patient [2,6–9]. Undoubtedly, direct trauma to this region or to the sinus node artery is associated with the *early appearance* of brady–tachydysrhythmias, as seen in our patients in group A. Modification of the surgical techniques does have a significant effect on decreasing the *early appearance* of these dysrhythmias. However, patients in sinus rhythm during initial follow–up are at continued risk to develop progressive sinus node dysfunction or atrial flutter years later.

Supraventricular tachycardia.

It has been our experience that atrial flutter and supraventricular tachycardia are poorly tolerated in the postoperative Mustard patient. Although the relative risk of atrial flutter is low, it can be life–threatening in these patients [10]. For that reason, we prophylactically continue all postoperative Mustard patients on digoxin indefinitely.

Mechanisms.

The causes of these late occurring dysrhythmias are only speculative. Bharati and Lev [11] described the late appearance of diffuse thickening of

the right atrium in autopsy specimens of postoperative Mustard patients. This was speculated to be secondary to blocked lymphatics. It is unknown if these progressive changes adversely affect the sinus node. Another possibility is progressive occlusion of the SAN artery. Loeb et al. [12] have used chronic embolization of the sinus node artery to reproduce in dogs many of the dysrhythmias seen in postoperative Mustard patients. Yet to be explored are changes induced by the altered hemodynamics from the redirected blood flow.

Invasive electrophysiologic studies may be predictive of later problems [7,13]. Symptoms of dizziness, syncope, or palpitations must be thoroughly investigated to exclude the sick sinus syndrome. Recent technologic improvements have made endocardial and epicardial permanent pacing a realistic therapeutic modality for selected patients in the pediatric age group [14,15].

Postoperative assessment.

Our routine follow–up of the postoperative Mustard patient now includes several ECGs and one 24–hour cardioscan prior to discharge. In addition, we perform an electrophysiology study and a second 24–hour scan 1 year postoperatively. Our data have shown a significant correlation between an abnormal sinus node recovery time and later dysrhythmias [7]. Treadmill testing will detect abnormal sinus node function in a large percentage of patients, but we were unable to correlate this with later dysrhythmias [16]. We then perform ECGs and 24–hour ECGs every 3 years. The importance of continued close observation is clear from the results of this study.

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CHAPTER 4

THE ASYMPTOMATIC CHILD A LONG TIME AFTER THE MUSTARD OPERATION FOR TRANSPOSITION OF THE GREAT ARTERIES

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THE ASYMPTOMATIC CHILD A LONG TIME AFTER THE MUSTARD OPERATION FOR TRANSPOSITION OF THE GREAT ARTERIES

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ABSTRACT

We studied 36 asymptomatic children 7.7 ± 2.5 years after a Mustard operation. Fifteen children had sinus rhythm on all electrocardiograms made during follow–up. Only 2 had normal 24–hour Holter recordings throughout follow–up, 6 had periods of supraventricular tachycardia, and 3 had periods of atrial flutter. The electrophysiological evaluation of sinus node function was normal in 5 of the 31 children who were studied. The behavior of the atrial myocardium was electrophysiologically abnormal in most of the children. Atrioventricular node function, on the contrary, was normal in nearly all of the children. Eleven children had normal hemodynamics. Four had severe or complete obstruction of the superior vena cava, 1 had a severe pulmonary venous obstruction, 3 had a severe left ventricular outflow tract obstruction, and 2 had a large left–to–right shunt. Only 3 children had normal hemodynamic and electrophysiological studies. We conclude that the absence of symptoms and a normal routine examination of children a long time after a Mustard operation does not exclude hemodynamic and electrophysiological abnormalities, which can sometimes be severe. In view of these disappointing results, we decided to replace the Mustard operation with the arterial switch operation in children with transposition of the great arteries.

INTRODUCTION

Since 1964 when Mustard [1] described the venous switch operation, the life expectancy and the quality of life of many children with transposition of the great arteries have improved. The operative mortality was extremely low, and the early results were good. After long–term follow–up, however, many problems were encountered; caval obstruction, pulmonary venous obstruction, tricuspid insufficiency, and right heart failure [2–5]. A high incidence of supraventricular arrhythmias and sinus node dysfunction has been reported, as well as a high incidence of sudden death, perhaps as a result of these arrhythmias [6–8].

Between 1969 and 1984, we [9] performed the Mustard operation in our hospital in 83 children with transposition of the great arteries. There have been no operative deaths for simple transposition of the great arteries since 1977 and for complex transposition since 1980; however, late mortality has been high. Eight children died suddenly and unexpectedly. There was a strong correlation with the presence of tachyarrhythmias; 7 of these 8 children had periods of atrial flutter compared with 16% of the whole group ($p < 0.01$). Although 8 children required reoperation and 5 required implantation of a pacemaker, the remaining children have done very well.

We wanted to know more about this group of asymptomatic children. Therefore, we studied 36 of them by means of hemodynamic and electrophysiological heart catheterization. All 36 had undergone a Mustard operation more than 4 years before. The results of the study are presented here.

MATERIAL AND METHODS

Patients.

Thirty–six asymptomatic children who had undergone a Mustard operation more than 4 years prior to the present study (mean ± SD, 7.7 ± 2.5 years) formed the study group. Based on the physical examination, 12–lead electrocardiogram (ECG), and chest roentgenogram, there was no suspicion of severe hemodynamic or electrophysiological abnormalities. Children who showed only a diminished capacity to perform competitive sports were included in the study.

Operative Technique.

All the children were operated on using cardiopulmonary bypass and hypothermia. Since 1977, the superior vena cava (SVC) and inferior vena cava have been selectively cannulated and cold cardioplegia has been used.

Table I. Patient characteristics of the three groups [a]

Variable	Total N=36	Group 1 N=16	Group 2 N=10	Group 3 N=10
Follow–up [b]	4–12 (7.7)	6–12 (10)	4–9 (6.5)	4–6 (5.1)
Age at operation [b]	2 ds–7.4(1.9)	0.7–5.6(3)	0.7–7.4(1.6)	2 ds–1.1(0.5)
VSD				
Large	1	–	1	–
Small	9	3	4	2
LVOTO	10	4	4	2
PDB	7	2	2	3

[a] Numbers in parentheses are mean values; [b] Data are shown in years unless otherwise indicated.
LVOTO = left ventricular outflow tract obstruction; PDB = persistent ductus of Botallo; VSD = ventricular septal defect.

Dacron was used as baffle material in all of the children; since 1979, the baffle has been "trouser shaped" according to the method of Quaegebeur and Brom [10]. The coronary sinus drained into the pulmonary venous atrium. The pulmonary atrium was enlarged with a pericardial patch in 10 children. Previous procedures included a Blalock–Hanlon atrial septectomy in 7 children.

To judge the possible effect of surgical modifications, we divided the children into three groups based on changes in surgical policy. In group 1, the operations took place between 1969 and 1977, and were performed mainly in children older than 1 year. In group 2, the operations occurred between 1977 and 1980, and were done using cold cardioplegia and selective cannulation of the caval veins. In group 3, the operations were done between 1980 and 1984 in children younger than 1 year. The data on age, follow–up, and associated anomalies are in Table I.

Study Protocol.

All postoperative ECGs and 24–hour Holter recordings were reviewed. The ECGs were made at least once a year, and the 24–hour Holter recordings were made every 1 or 2 years. The mean number of 24–hour Holter recordings per patient was 4.7 ± 3. Seventeen children (47%) performed an exercise test with a bicycle ergometer according to the protocol described by Godfrey and colleagues [11]. A two–dimensional and Doppler echocardiogram was made on the day of the catheterization.

Cardiac Catheterization.

After the parents gave informed consent and after approval by the institution's committee of clinical investigation, all of the children underwent hemodynamic and electrophysiological catheterization. Most of the children were sedated with meperidine hydrochloride, 2 mg/kg of body weight, and promethazine, 1mg/kg of body weight, administered intramuscularly. Eight children older than 12 years were sedated with diazepam given orally. The catheter was introduced percutaneously into a femoral vein and artery. In 6 patients in whom both the femoral and iliac veins were occluded, the internal jugular vein was entered percutaneously under general anesthesia.

Hemodynamic study. Besides the usual pressure and oxygen saturation measurements, withdrawal pressures were registered from the SVC to the inferior vena cava through the systemic venous atrium and from the main pulmonary artery to the left ventricle. The pulmonary wedge pressure was measured simultaneously with either the pressure in the pulmonary venous atrium or the right ventricular end–diastolic pressure. Cardiac index and shunt calculations were made by the dye–dilution technique. Biplane cineangiograms were made with contrast injections in the SVC and both ventricles. Volumes were calculated from the biplane angiogram utilizing Simpson's rule method [12].

Electrophysiological study. An electrophysiological study could be performed in 31 children. A 5 F quadripolar catheter was placed at the junction between the SVC and the systemic venous atrium. Four surface ECGs (I, II, aVF, and V1) and the femoral arterial pressure were recorded throughout the study. Recordings were performed with a Siemens–Elema Mingograph with a paper speed of 100 or 250 mm/s. A Medtronic 5325 stimulator was used for pacing. The amplitude of the stimuli delivered was twice the threshold with a pulse width of 1.8 ms. Electrophysiological measurements included the following: corrected sinus node recovery time [13], sinoatrial conduction time [13], AV node Wenckebach response to atrial pacing, and effective refractory periods of the atrium and AV node. Values more than two standard deviations above the mean value for children with normal hearts were considered abnormal [14,15].

Statistical Analysis.

Statistical analysis was performed with the χ^2 test. A p value of less than 0.05 was considered significant. Results were expressed as the mean $\pm$ one standard deviation.

Table II. Children with specific rhythm or arrhythmia on electrocardiograms and 24–hour Holter recordings made during follow–up (N = 36)

Variable	ECG	Holter
Sinus rhythm	15 (42%)	2 (6%)
AV junctional rhythm	18	21
Atrial rhythm	6	6
Sinus arrest	3	12
SVT	–	6
Atrial flutter	3	3
PAC	3	13 [a]
PVC	–	3 [a]

[a] These patients had more than ten contractions per hour.
AV = atrioventricular; ECG = electrocardiogram; PAC = premature atrial contraction; PVC = premature ventricular contraction; SVT = supraventricular tachycardia.

RESULTS

Electrocardiogram.

Fifteen children (42%) were in sinus rhythm during the entire follow–up period (Table II). Although the incidence of sinus rhythm was the highest in group 3 (60%), the differences between the three groups were not significant. Eighteen children had at least one period of AV junctional rhythm on their ECG, alternating with atrial rhythm or atrial flutter in 6 children.

24–hour Holter Recording.

Only 2 (6%) children had no abnormalities on all of their 24–hour Holter recordings (see Table II). The periods of sinus arrest were longer than 1.8 s in 6 children. (Sinus arrest up to 1.8 s is also seen in healthy children [16].) Most children had more than one type of arrhythmia during follow–up. The incidence and type of arrhythmias did not differ significantly between the three groups. However, atrial flutter was present only in group 1.

Exercise Test.

The exercise capacity ranged from 59 to 100% (mean capacity, 75%) of normal for length and sex. Premature atrial contractions developed in 3 children during exercise; 2 remained in AV junctional rhythm throughout the exercise test.

Echocardiogram.

A complete two–dimensional and Doppler echocardiogram was obtained in 26 of the 36 children. An obstruction of the systemic venous return was

Table III. Results of hemodynamic studies in the three groups

Variable	Total N = 36	Group 1 N = 16	Group 2 N = 10	Group 3 N = 10
Normal	11 (31%)	6	1	4
SVC obstruction				
5–10 mm Hg	4	1	2	1
> 10 mm Hg	4	3	1	–
IVC obstruction				
5–10 mm Hg	2	1	–	1
> 10 mm Hg	–	–	–	–
PV obstruction				
5–10 mm Hg	5	2	1	2
> 10 mm Hg	1	–	1	–
LVOTO				
25–50 mm Hg	4	2	1	1
> 50 mm Hg	3	1	1	1
Baffle leakage				
< 25%	8	2	4	2
> 25%	2	–	2	–
Tricuspid insufficiency	2	–	1	1
Cardiac index (l/min/m^2)	3.3 ± 0.7	3.5 ± 1.8	3.1 ± 0.4	3.2 ± 0.7

IVC = inferior vena cava; LVOTO = left ventricular outflow tract obstruction; PV = pulmonary venous; SVC = superior vena cava.

suspected by pulsed Doppler echocardiography because of nonphasic disturbed blood flow during diastole in 6 of the 9 patients with substantial pressure gradients at cardiac catheterization. A complete echocardiogram was available for 4 patients with pulmonary venous channel stenosis, all demonstrating a narrowed channel (less than 11 mm), with flow disturbance in the inflow of the atrium. A major left ventricular outflow tract obstruction was detected by echocardiography in all 7 patients with pressure gradients higher than 25 mm Hg at cardiac catheterization. Baffle leak flow was demonstrated in 4 patients and was missed in 4, in whom the shunt was less than 25% of the pulmonary circulation.

Hemodynamic Study.

No hemodynamic abnormalities were found in 11 children (31%) (Table III). The rest often had more than one abnormality. We found no significant differences between the three groups in the incidence of hemodynamic

abnormalities separately or combined. In group 3, however, no severe baffle obstructions were found.

Caval obstructions. In 4 children, the obstruction was severe (greater than 10 mm Hg) or complete. All of the children had a good runoff through the azygos vein to the inferior vena cava. None of the children with a SVC obstruction had a protein–losing enteropathy.

Pulmonary venous obstruction. A pressure difference of more than 10 mm Hg between the pulmonary artery wedge pressure and either the right ventricular end–diastolic pressure or the pulmonary venous atrial pressure was found in 1 child. Of the 10 children in whom the pulmonary venous atrium was enlarged, 1 had a moderate pulmonary venous obstruction.

Left ventricular outflow tract obstruction. Of the 7 children with left ventricular outflow tract obstruction, 6 had pressure differences over the left ventricular outflow before operation. The stenosis remained the same in 4 and increased in 2. In 4 children with a preoperative obstruction, the pressure difference disappeared after the Mustard operation.

Baffle leakage. The leakage was located mostly in the vicinity of the SVC or inferior vena cava. The left–to–right shunt constituted more than 25% of the pulmonary flow in 2 children.

Tricuspid insufficiency. Two children showed moderate tricuspid insufficiency on the right ventricular cineangiogram.

Cardiac function. One child had a cardiac index lower than 2.5 l/min/m^2. Right ventricular ejection fraction could be measured in 13 children. The mean ejection fraction was 57% ± 12%. Three children had an ejection fraction lower than 45%.

Electrophysiological Study.

An electrophysiological study could be performed in 31 children (Table IV). Nonsustained tachycardia from atrial pacing or from atrial extrastimuli given during sinus rhythm developed in 10 children (32%): supraventricular tachycardia in 6; atrial flutter in 3; and a wide QRS tachycardia, possibly of ventricular origin, in 1. The correct electrophysiological mechanism could not be analyzed because only one electrode catheter was used.

The number and the severity of the electrophysiological abnormalities did not differ significantly between the three groups (see Table IV). Of the 11 children in whom no hemodynamic abnormalities were found, 4 had severe abnormalities of the sinus node. These abnormalities were detected during the electrophysiological study as well as in the 24–hour Holter recordings. Four others had moderately abnormal electrophysiological studies and arrhythmias. Only 3 children had both normal hemodynamic and electrophysiological studies.

Table IV. Electrophysiological results in the three groups

Variable	Total	Group 1	Group 2	Group 3
CSNRT (N = 31)				
< 275 ms	5 (16%)	1	2	2
275–550 ms [a]	15	9	2	4
> 550 ms [a]	11	4	4	3
Secondary pauses [a]	8	5	1	2
Abnormal escape [a]	16	10	3	3
Entrance block [a]	8	3	2	3
Atrial standstill	1	1	–	–
SACT (N = 24)				
< 200 ms	6	2	3	1
> 200 ms [a]	4	1	1	2
Not determinable	14	7	1	6
Wenckebach (N = 31)				
< 350 ms	27 (87%)	13	6	8
> 350 ms [a]	4	1	2	1
AVERP (N = 27)				
Normal [b]	26 (96%)	11	6	9
Prolonged [a]	1	–	1	–
AERP (N = 27)				
Normal [b]	10 (37%)	5	2	3
Prolonged [a]	17	6	5	6

[a] A statistical analysis was done, and there was no significant difference between groups.
[b] Normal values are dependent on cycle length.
AERP = atrial effective refractory period; AVERP = atrioventricular node effective refractory period; CSNRT = corrected sinus node recovery time; SACT = sinoatrial conduction time.

Sinus node. The response of the sinus node to atrial pacing was very abnormal in most of the children. The corrected sinus node recovery time was within the normal range in only 5 children (16%). In 2 of these children, this could have been due to an entrance block of the sinus node. The corrected sinus node recovery time was moderately abnormal in 15 and severely abnormal in 11 with a maximal time of 2,690 ms. More striking was the abnormal behavior of the sinus node. Secondary pauses were seen in 8 children, abnormal escape rhythm in 16, and entrance block in 8. In 1 child with AV junctional escape, an atrial standstill of 28 seconds was found. In 14 children, the sinoatrial conduction time could not be calculated either because of non–reset of the sinus node or the presence of pronounced sinus arrhythmia.

Atrioventricular node. Atrioventricular node function was normal in most of the children.

Atrium. The atrium reached refractoriness before the AV node in 72% of the children. Only 20% of normal children show this phenomenon [14].

Late Deaths.

Three children died suddenly during follow–up after cardiac catheterization. One child had normal hemodynamics but severe abnormalities of the sinus node with periods of atrial flutter on the 24–hour Holter recordings. She died during exercise, despite having an AAI pacemaker and receiving antiarrhythmic drug treatment. The other 2 children had a pulmonary venous obstruction with a pressure difference between 5 and 10 mm Hg. One of them also had periods of atrial flutter.

COMMENT

The results of this study show that most children who have undergone a Mustard operation, even if they are asymptomatic and seem to be doing well, have major hemodynamic and electrophysiological abnormalities. We cannot predict what the consequences of these findings will be for the children we studied, who are asymptomatic at present. Obstruction of the SVC is well tolerated if there is good collateral venous drainage; however, problems (due to intestinal lymph congestion, for example) can be expected. If moderate pulmonary venous obstruction is present in childhood, progressive narrowing with growth seems probable. A residual left–to–right shunt will possibly, by its volume load, increase the chance of arrhythmias developing in the already compromised atrium. We, therefore, believe that hemodynamic problems can be expected in these asymptomatic children in the future.

Hayes and Gersony [17] and Duster and associates [18] reported that the incidence of arrhythmias increased with longer follow–up. Therefore, it can be anticipated that the arrhythmias and the electrophysiological abnormalities in our patients will worsen and probably will become symptomatic with a much longer follow–up. Southall and co–workers [19] cautioned that the incidence of arrhythmias created by operative intervention should not be overestimated, because children with normal hearts also show arrhythmias on 24–hour Holter recordings and because arrhythmias are already present preoperatively in some children with congenital heart disease. We did not perform 24–hour Holter recordings preoperatively, but all the children had sinus rhythm preoperatively on the surface ECG compared with 42% postoperatively. The arrhythmias detected on the 24–hour Holter recordings were more severe than those described by Southall and colleagues [16] in normal children. Atrioventricular junctional rhythm was seen for several hours, and

occasionally throughout most of the 24 hours. Only more than ten premature beats per hour was considered abnormal. Supraventricular tachycardia and atrial flutter, as found in our patients, are not seen in healthy children. Therefore, we believe we do not overestimate the incidence of arrhythmias after the Mustard operation.

Many surgical modifications have been described to reduce the incidence of hemodynamic and electrophysiological problems after the Mustard operation [20–22]. Many of these modifications, eg, selective SVC cannulation, the trouser–shaped patch, and superficial stitching around the sinus node area, have been applied in our hospital. Despite this, the hemodynamic and electrophysiological results did not improve significantly, as shown by comparison of the three surgical groups. Atrial flutter was seen only in group 1, but this is as likely to be the result of the longer postoperative period [17,18] as the result of the changes in surgical technique. The absence of severe baffle obstructions in group 3 can likewise be explained by the shorter postoperative period.

The incidence of sudden death was very high in our patients compared with the incidence of sudden death reported in the literature [6]. Deanfield and associates [23] found no correlation between the presence of arrhythmias and sudden death in their prospective study. Three of our children died during follow–up after catheterization. Two of them had periods of atrial flutter, as did 7 out of 8 children who died suddenly before the study was started. Unlike Deanfield and colleagues [23], we found that atrial flutter seemed to increase significantly the risk of sudden death in our patients. Of the 3 children who died in our series, 1 was not known to have atrial flutter. The other 2 died during exercise or during proven tachycardia. Ventricular fibrillation as a result of 1 : 1 conduction of atrial flutter could well have been the cause of sudden death in these children.

The arterial switch operation, presented in 1975 by Jatene and co–workers [24] as an anatomical correction for transposition of the great arteries, had such a high operative mortality at first that it was not then an alternative for the Mustard operation. However, the operative mortality of the arterial switch operation has decreased considerably during recent years. Quaegebeur and colleagues [25] and Radley–Smith and Yacoub [26] reported a 12% and 9% operative mortality, respectively. Late mortality was 5% and 0%, respectivily. Although much fewer data are available on the long–term follow–up of the arterial switch operation than on the Mustard operation, it seems that arrhythmias are rare and hemodynamic problems are less frequent than after Mustard's operation [25–28].

We conclude that even children who seem to be doing well a long time after a Mustard operation have unexpected electrophysiological and hemodynamic abnormalities that could well deteriorate during further follow–up. Moreover, the results point out that the absence of symptoms combined with no or minor abnormalities at the physical examination and on the ECG and chest roentgenogram do not mean that the child is really well. Only cardiac catheterization and repeated 24–hour Holter recordings together with two–dimensional and Doppler echocardiography can exclude abnormalities. Considering the disappointing results of the Mustard operation as shown in this study, and in view of the recent encouraging results of the arterial switch operation, we considered it justified at our institution to replace the Mustard operation with the arterial switch operation for children with simple and complex transposition of the great arteries.

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CHAPTER 5

FUNCTIONAL ABNORMALITIES OF THE CONDUCTION SYSTEM IN CHILDREN WITH SECUNDUM ATRIAL SEPTAL DEFECT

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FUNCTIONAL ABNORMALITIES OF THE CONDUCTION SYSTEM IN CHILDREN WITH SECUNDUM ATRIAL SEPTAL DEFECT

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SUMMARY

We performed an electrophysiologic study in 40 children with an atrial septal defect and analyzed their pre– and postoperative electrocardiograms and 24–hour Holter recordings. The electrophysiologic study showed a prolonged corrected sinus node recovery time in 83% and an abnormal sinoatrial conduction time in 25% of the children. An early Wenckebach response to atrial pacing was seen in 18%. Sixteen percent had a prolonged atrial conduction time. The atrial functional refractory period was abnormal in 35%. Two children developed nonsustained supraventricular tachycardia during the electrophysiologic study. The preoperative electrocardiogram showed first–degree atrioventricular block in 15% of the children; prolonged periods of accelerated atrial rhythm were found in 35% of the preoperative 24–hour Holter recordings. The incidence of first–degree atrioventricular block and accelerated atrial rhythm decreased postoperatively. We could not find a significant correlation between age or shunt size and the presence of electrophysiologic abnormalities or arrhythmias. These results indicate that the sinus node, atrioventricular node and atrial myocardium show some degree of dysfunction in patients with an atrial septal defect. An early operation may prevent further progression of electrophysiologic abnormalities and the development of symptomatic arrhythmias.

INTRODUCTION

The incidence of supraventricular arrhythmias in adults with atrial septal defect is high. Although patients improve clinically after an operation at older age, they continue to have atrial fibrillation or supraventricular tachycardia [1,2]. This is one of the reasons why surgical treatment in childhood is advocated. After repair of an atrial septal defect, however, supraventricular arrhythmias are also common [3–5]. In a retrospective study of 204 children, operated on for atrial septal defect in our hospital, we found that 23% of the children had arrhythmias on their routine electrocardiogram after a mean follow–up of 2.3 years. Ten percent of the 204 children had arrhythmias of sufficient severity to require treatment or pacemaker implantation [6].

These arrhythmias can be caused by damage to the conduction system during surgery. The incidence of arrhythmias after closure of an atrial septal defect, however, seems to be higher than after, for example, repair of a ventricular septal defect. Another explanation may be that patients with an atrial septal defect are prone to supraventricular arrhythmias due to congenital or acquired abnormalities of the conduction tissue.

In 1982, Clark and Kugler [7] found signs of dysfunction of the sinus and atrioventricular nodes in a small group of children with atrial septal defect. We decided to study this in a larger group of children and included electrophysiologic studies of both nodes in our preoperative catheterization protocol for patients with an atrial septal defect. We report in this paper the results of these studies in 40 infants and children [8,9]. In all the children undergoing operation, we reviewed the electrocardiograms and 24–hour Holter recordings made preoperatively and 3 months and 1 year after the pocedure so as to correlate any observed electrophysiologic abnormalities with the clinical arrhythmias.

METHODS

Patients.

We studied 40 non–selected and consecutive patients with an atrial septal defect aged 0.8–16.8 years (mean 6.8 years). None of the children complained of palpitations, dizziness or syncope. All the children underwent a routine preoperative evaluation with a standard 12–lead electrocardiogram, 24–hour Holter recording, echocardiogram and a hemodynamic cardiac catheterization in which an electrophysiology protocol was included for the period of this study. The study was approved by the institution's committee of clinical investigation and informed consent was obtained from the patient's parents.

Cardiac Catheterization.

Premedication. Meperidine 2 mg/kg of body weight and promethazine 1 mg/kg were administered intramuscularly to most children. Six older children received 5–10 mg diazepam orally. In 11 of the 18 children younger than 5 years, we used thiopental 35 mg/kg rectally (see Results).

Hemodynamic study. Flows and shunt size were calculated from dye dilution curves or from measured oxygen consumption and saturations according to the Fick principle. If cineangiography was necessary, it was performed after the electrophysiologic study.

Electrophysiologic study. In most of the children, one electrode catheter was successively placed at the right ventricular apex, His bundle region and the high right atrium. Only in children older than 5 years were two catheters used at the same time. For recording of the His (atrioventricular) bundle, a 5 French tripolar catheter was used, and for atrial and ventricular recordings a 5 French quadripolar catheter. Four surface electrocardiograms I, II, aVF, V1 and the femoral arterial pressure were recorded throughout the study. Recordings were performed with a Siemens–Elema Mingograph at a paper speed of 100 or 250 mm/sec. A Medtronic 5325 stimulator was used for pacing. The amplitude of the stimuli delivered was twice the threshold with a pulse width of 1.8 msec. Electrophysiologic measurements included: resting intervals, corrected sinus node recovery time [10], sinoatrial conduction time according to Strauss (in [10]), sinoatrial conduction time according to Narula [11], atrioventricular node Wenckebach response, effective and functional refractory periods of the atrium and atrioventricular node. Values more than 2 standard deviations above the mean value for children with normal hearts [12,13] were considered abnormal.

Electrocardiogram and 24–Hour Holter Recording.

Twelve–lead electrocardiograms were made for all the children. From those children, who had to have surgery, the pre– and postoperative electrocardiograms were analyzed. Likewise, 24–hour Holter recordings were made preoperatively and 3 months and 1 year postoperatively. Accelerated atrial rhythm was defined as a supraventricular rhythm with an abnormal P vector and a rate higher than the age adjusted value for atrial escape rhythm [14].

Statistics.

For statistical analysis χ^2 test, Fisher's exact test and Student's t test were used. A p value of < 0.05 was considered significant.

Table I. The influence of premedication on the electrophysiologic data

	Meperidine Promethazine	Thiopental	
Age (years)	3.8 ± 1.1	2.8 ± 1.0	NS
QP (l/min per m^2)	8.0 ± 3.0	9.7 ± 3.9	NS
CSNRT (msec)	439 ± 58	261 ± 61	$p < 0.001$
SACT (msec)	150 ± 63	153 ± 18	NS
AERP (msec)	205 ± 28	198 ± 23	NS

AERP = atrial effective refractory period; CSNRT = corrected sinus node recovery time; NS = not significant; QP = pulmonary blood flow; SACT = sinoatrial conduction time.

RESULTS

Hemodynamic study.

Six patients had a sinus venosus type defect while 7 had partially anomalous pulmonary venous return. The Qp/Qs ratio ranged from 1.2 : 1 to 5 : 1 (mean 2.5). The pulmonary blood flow ranged from 3.2–19.7 (mean 7.9) l/min per m^2. No additional abnormalities were present, except a small pressure gradient over the pulmonary valve in 2 patients.

Electrophysiologic study.

Influence of premedication. Of the 18 children younger than 5 years, 7 were premedicated with meperidine and promethazine; 11 received thiopental. The children premedicated with thiopental were younger, but the age difference between the two groups was not significant. There was also no significant difference in shunt size. The corrected sinus node recovery time, however, was significantly shorter in children premedicated with thiopental ($p < 0.001$). There was no significant difference in the other electrophysiologic data between the two groups (Table I). The known normal values of corrected sinus node recovery time, taken from the literature, are from children premedicated with meperidine and promethazine. We, therefore, excluded from our results the corrected sinus node recovery time values from children who received thiopental as premedication. Sedation with diazepam is known to have no major electrophysiologic effects [15].

Resting intervals. The interval between the high right atrial depolarization or the P wave and the low right atrial depolarization was prolonged in 5 of 31 children (16%), in whom it was measured. The interval between the low right atrium and the His bundle deflection and the His to ventricle interval were both prolonged in 1 of 33 children (3%). The conduction time through the

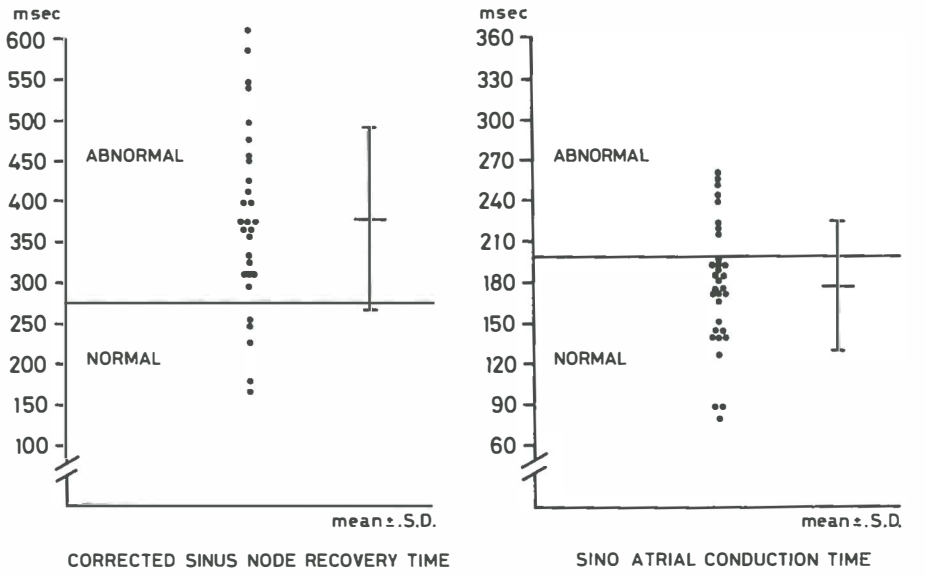

Figure 1. Corrected sinus node recovery time (n=29) and sinoatrial conduction time according to Strauss (n=32) in children with atrial septal defect. The horizontal line indicates the upper normal limit according to Kugler [10].

right bundle was prolonged in only 1 of 29 children (3%) with RSR' pattern in the right precordial leads of the surface electrocardiogram.

Sinus node (Fig. 1). The corrected sinus node recovery time was abnormal in 24 of 29 children (83%). The data from the children sedated with thiopental were excluded. The maximal corrected sinus node recovery time was 610 msec. We saw no secondary pauses or abnormal escape rhythms. The sinoatrial conduction time according to Strauss was prolonged in 8 of 32 children (25%). All the children had a normal reset response. Sinoatrial conduction time measured according to Narula showed such different return intervals in consecutive measurements that we decided to ignore these data.

Atrium (Fig. 2). The effective refractory period of the atrium was normal in all the children. In 28 of 37 (76%) of the patients, the atrium reached refractoriness before the atrioventricular node. Normally this happens in only about 20% of children [12]. The functional refractory period of the atrium was abnormal in 6 of the 17 patients (35%) in whom it was measured. During the electrophysiologic study, 2 children developed nonsustained supraventricular tachycardia.

Atrioventricular node (Fig. 3). The effective refractory period was normal in all the children. The functional refractory period was abnormal in only 2 of

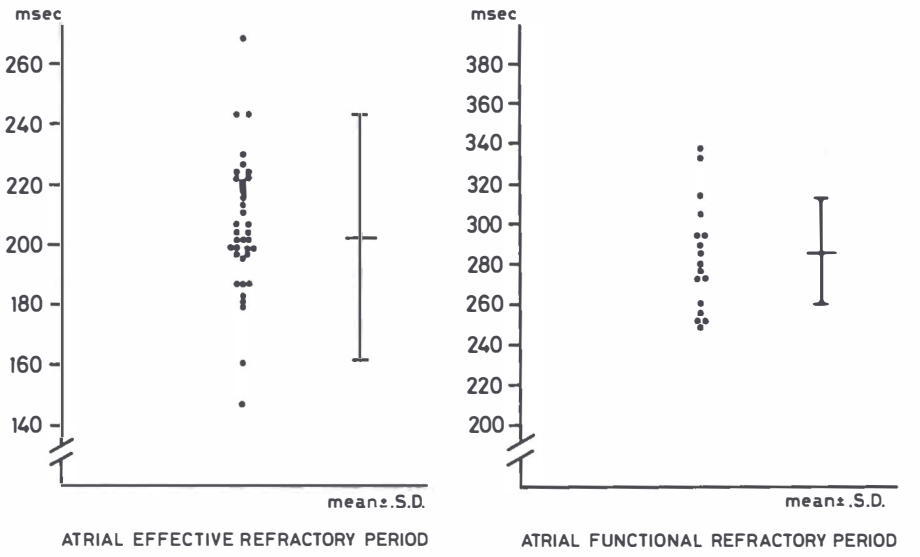

Figure 2. Atrial effective (n=37) and functional refractory period (n=17) in children with atrial septal defect.

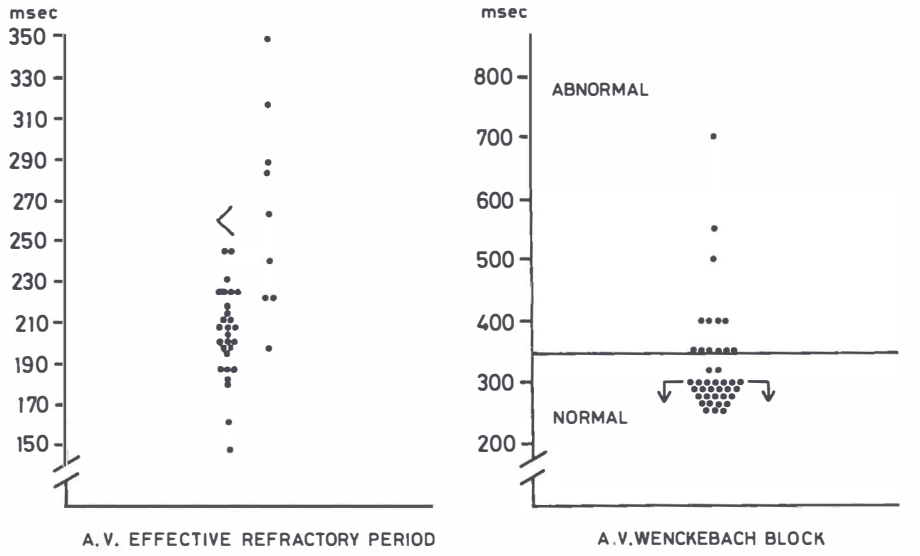

Figure 3. Effective refractory period of the atrioventricular node (n=37) and Wenckebach response to atrial pacing (n=40). The effective refractory period of the atrioventricular node could not be measured exactly in 28 patients because the atrium reached refractoriness earlier. The horizontal line indicates the upper normal limit according to Gillette et al. [12].

Table II. Pre– and postoperative 24–hour Holter recordings

	Preoperative N = 31	Postoperative N = 31
Abnormal Holter recordings	14	8
Accelerated atrial rhythm	11	6
AVJ rhythm	1	2
Sinus arrest	2	–
2nd degree AV block		
type I	1	–
type II	2	–
PACs > 10 / hr	1	1
PVCs > 10 / hr	–	1

AVJ = atrioventricular junctional; PAC = premature atrial contraction; PVC = premature ventricular contraction.

the 35 children (6%). A Wenckebach second–degree block developed too early in 7 of 40 children (18%).

We did not find a significant correlation between any of the electrophysiologic parameters, alone or combined, and age or shunt size.

Electrocardiogram.

Six children had first–degree atrioventricular block (15%). This was due to an abnormally prolonged atrial conduction alone in one child, and in another to a combination of a prolonged atrial conduction time with an abnormal His to ventricle conduction. In a third child, an abnormal prolonged atrioventricular node conduction was the cause of the first–degree atrioventricular block. All the others showed combinations of prolonged, but not abnormal, conduction through the atrium, atrioventricular node or bundles. The first–degree block disappeared postoperatively in 5 of 6 children ($p = 0.05$).

24–Hour Holter Recording.

Fourteen of the 31 preoperative Holter recordings showed some arrhythmias (Table II). The high incidence of prolonged periods of accelerated atrial rhythm was striking (35%). The periods lasted for at least 30 minutes, but often for hours. These children were older (9.7 years) than the children without accelerated atrial rhythm (5.9 years), but this difference did not become significant, nor was there any significant relation found to shunt size or any electrophysiologic parameter.

Eight of the 24–hour Holter recordings made 1 year postoperatively showed some arrhythmias (Table II). The number of children with accelerated atrial rhythm decreased postoperatively from 11 to 6, but this difference was

not significant. Only 1 child developed accelerated atrial rhythm, all the others already had it preoperatively. Again, we found no correlation between postoperative arrhythmias and age, shunt size or any specific electrophysiologic abnormality. All pre– and postoperative arrhythmias caused no symptoms and were of little clinical importance.

DISCUSSION

Our results confirm the findings of Clark and Kugler [7]. We found that children with atrial septal defects have abnormal parameters of sinus nodal function and, to some extent, abnormal function of the atrioventricular node. Furthermore, electrophysiologically, the atrial myocardium behaves abnormally. The surface electrocardiogram shows a high incidence of first–degree atrioventricular block and the 24–hour Holter recording demonstrates a high incidence of accelerated atrial rhythm, both decreasing after operation. The arrhythmias were of little clinical importance. Some of the arrhythmias, found on the 24–hour Holter recording, are also seen in healthy children, but are then less frequent and less prolonged [16]. We found no correlation between the presence of electrophysiologic abnormalities and the incidence or type of arrhythmias.

The abnormal behavior of the conduction system could be congenital in children with an atrial septal defect, since the development of the conduction tissue and the atria are closely related [17]. It seems more likely, however, that the abnormalities in electrophysiology are caused by the prolonged volume load, stretching the atrial wall and the adjacent conduction tissue. It may well be that the changes we observed in children represent the beginning of the mechanism which causes atrial fibrillation and supraventricular tachycardia in adults with uncorrected atrial septal defects. In favor of this hypothesis is the decrease in first–degree atrioventricular block and accelerated atrial rhythm seen postoperatively in our study. In addition, Bolens and Friedli [18] and Karpawich et al. [19] found an improvement of sinus and atrioventricular nodal function after repair of atrial septal defects in children studied pre– and postoperatively. If the volume load of the right atrium is the main factor, one would expect the electrophysiologic abnormalities to progress with age and to correlate to shunt size. We found no such correlation in our study. Other authors, however, did find a relation to age [7,20] or shunt size [7]. We had to exclude the results of the corrected sinus node recovery time of 11 children younger than 5 years because of premedication with thiopental. This could be the reason why we did not find a correlation with age.

The incidence of postoperative arrhythmias found on the electrocardiogram and 24–hour Holter recording is less than we reported previously in our institution [6]. This is due to a change in cannulation technique from cannulation of the superior caval vein through the right atrial appendage to its selective cannulation [25]. The arrhythmias which occur after repair of an atrial septal defect, therefore, seem to be due at least in part to surgical damage to the conduction system, and probably partly to the electrophysiologic abnormalities described in this paper.

We cannot conclude from our study alone that the electrophysiologic abnormalities will worsen with age and will diminish after closure of the atrial septal defect. The postoperative improvement found by others [18,19], however, and the decrease of first–degree atrioventricular block and accelerated atrial rhythm postoperatively in our study, may at least be another argument in favor of closure of the atrial septal defect at an early age. Several authors [21–24] reported a varying incidence of between 14 and 55% of spontaneous closure of atrial septal defect in young children. Early operation on asymptomatic patients with an atrial septal defect, therefore, carries the risk of operating children unnecessarily. Considering that most atrial septal defects close spontaneously in the first years of life, we advise that repair of an atrial septal defect be done when the patient is between 4 and 5 years of age.

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CHAPTER 6

ARRHYTHMIAS AFTER REPAIR OF SECUNDUM ATRIAL SEPTAL DEFECT: THE INFLUENCE OF SURGICAL MODIFICATION

American Heart Journal 1988;115:629–633

ARRHYTHMIAS AFTER REPAIR OF SECUNDUM ATRIAL SEPTAL DEFECT: THE INFLUENCE OF SURGICAL MODIFICATION

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SUMMARY

A retrospective study performed in our institution showed a significant correlation between venous cannulation and the incidence of arrhythmias after atrial septal defect (ASD) repair. We now report the results of a prospective study in 50 children operated on for ASD with selective cannulation of the superior vena cava. ECGs and Holter recordings were made before and after surgery, with a mean follow–up of 2.6 years. We found a significant decrease in postoperative arrhythmias ($p < 0.05$) after changing the cannulation technique. Severe arrhythmias, present in 10% of the children in the retrospective group, were not found in the prospective study. Six children had asymptomatic arrhythmias on the Holter recording 1 year after surgery. Three of them, however, already had arrhythmias before the operation. We conclude that the incidence and severity of arrhythmias after ASD repair can be reduced significantly by surgical modifications, at least for the follow–up period of this study. The long–term significance has to be awaited.

INTRODUCTION

Adults with secundum atrial septal defect (ASD) often have paroxysmal supraventricular arrhythmias [1,2]. The reason for recommending surgical closure in childhood, besides prevention of cardiac failure and pulmonary hypertension, is to prevent supraventricular arrhythmias arising when the patient becomes older. However, many authors also mention a high incidence of supraventricular arrhythmias after surgery for ASD in children [3–5]. Sinus node dysfunction after ASD closure actually constitutes 10 to 20% of the indications for pacing in childhood [6,7]. In 1983, we published the data of 204 ASD patients operated on in our hospital. We found a 23% incidence of postoperative arrhythmias in this group, compared with 2% preoperatively [8]. Ten percent of the 204 children showed severe arrhythmias requiring drug treatment or pacemaker implantation. As expected, a strong correlation was found between postoperative arrhythmias and the type of ASD and the presence of abnormal pulmonary venous drainage. Moreover, if the patient was operated on without cardiopulmonary bypass, i.e., by using hypothermia, the incidence of arrhythmias was significantly less ($p < 0.008$) than with cardiopulmonary bypass. We concluded that cannulation of the superior vena cava (SVC) through the right atrial appendage (RAA), as was used, could be one of the factors that caused the high incidence of arrhythmias by damaging the sinus node area or the sinus node artery. We therefore decided, in 1982, to change our cannulation technique to a selective cannulation of the SVC.

We then started a prospective study in 50 consecutive patients operated on for ASD, with the same period of follow–up as in the retrospective study. The results of this study are presented in this report. The aim of the study was first to judge if the modification of the cannulation influenced the incidence of postoperative arrhythmias during this period of follow–up and second to learn if arrhythmias, present before the operation, contributed to the postoperative arrhythmias.

METHODS

Patients.

We studied 50 consecutive patients operated on for ASD in our institution between 1982 and 1986; 21 were male and 29 were female. Their age at operation was between 1 and 17.5 years (mean 7.3 years). The follow–up was 0.6 to 5.6 years (mean 2.6 years). Forty–six children were followed more than 1 year. A sinus venosus type of ASD was present in six children (12%), and partial anomalous pulmonary venous drainage was observed in 11 (22%).

Table I. Patient data from both the retrospective and prospective study

	Retrospective N = 204 (%)	Prospective N = 50 (%)
Follow–up (years)	0.1–8.2 (2.3)	0.6–5.6 (2.6)
Age at operation (years)	0.1–17.2 (7.5)	1–17.5 (7.3)
Male : female	48% : 52%	42% : 58%
ASD		
Ostium secundum	78%	76%
Sinus venosus	10%	12%
Partial anomalous pulmonary venous return	22%	22%

ASD = atrial septal defect.

The Qp/Qs ratio ranged from 1.3 : 1 to 5 : 1 (mean 2.6 : 1). The mean pulmonary bloodflow was 8.7 l/min/m^2. Age at operation, duration of follow–up, and type of ASD did not differ significantly between the groups studied retrospectively and prospectively (Table I).

Study protocol.

All patients underwent a preoperative cardiac catheterization. Pulmonary blood flow was determined by dye dilution curves or by measurement of the oxygen consumption and saturations according to the Fick principle. In all children, pre– and postoperative ECGs were analyzed. At least four pre– and four postoperative ECGs were available. Twenty–four–hour Holter recordings were made preoperatively and at 3 and 12 months postoperatively. Accelerated atrial rhythm was defined as a supraventricular rhythm with an abnormal P vector and a rate higher than the age–adjusted value for atrial escape rhythm [9]. One year postoperatively, an exercise test was performed in 34 children with a bicycle ergometer according to the protocol described by Godfrey et al [10]. The data concerning arrhythmias were compared with those of the 204 patients from our retrospective study [8]. We only compared the ECGs, because no 24–hour Holter recordings were performed in the retrospective study.

Operative technique.

All patients were operated on with cardiopulmonary bypass with cold cardioplegia. The SVC and inferior vena cava (IVC) were selectively cannulated in all children by the use of 90–degree angulated cannulae. If the position of the sinus node artery allowed, the atrium was opened with a standard incision

Table II. The incidence of arrhythmias on pre– and postoperative ECGs in the retrospective and prospective study

	Retrospective N = 204 (%)	Prospective N = 50 (%)	*p* value
Preoperative			
Total period	2	8	< 0.05
Postoperative			
Total period	35	14	< 0.01
At end of follow–up	23	10	< 0.05
Severe arrhythmias	10	–	< 0.05
Pacemaker	2	–	NS

parallel to the coronary sulcus. The defect was closed with a Dacron patch in all but one patient. Pulmonary veins had to be redirected in 9 children.

Statistical analysis.

Comparison of arrhythmias was made by the χ^2 test and by Fisher's exact test. A p value of < 0.05 was considered significant.

RESULTS

Electrocardiogram.

Preoperative . First–degree atrioventricular (AV) block was seen in 11 children, right axis deviation was found in three, and left axis deviation was observed in two. RSR' configuration of the QRS complex was present in 36 patients. Four children (8%) showed arrhythmias on their preoperative ECGs. Two had accelerated atrial rhythm, one had premature atrial contractions (PACs), and one had a sinus arrest with an AV junctional escape rhythm.

Postoperative . The first–degree AV block disappeared after surgery in 10 out of 11 patients. Seven children (14%) showed arrhythmias on a routine ECG during the entire follow–up period. Five (10%) had arrhythmias at the end of the follow–up period. Two had an accelerated atrial rhythm, two had premature ventricular contractions (PVCs), and one had PACs. None of the children had severe arrhythmias, compared with 10% of the retrospective group ($p < 0.05$). Atrial flutter was not present in the prospective group, but was seen in 15 children (7%) in the retrospective study. The difference between the incidence of arrhythmias pre– and postoperatively in the prospective

Table III. Arrhythmias detected on pre– and postoperative 24–hour Holter recordings

	Preoperative	Postoperative	
		3 months	1 year
	N = 50	N = 50	N = 46
Atrial rhythm*	17	13	8
AVJ rhythm	4	2	3
Sinus arrest	3	3	–
2^{nd}–degree AV block			
Type I	2	–	–
Type II	3	–	–
PACs > 10/hr	3	3	4
PVCs > 10/hr	–	–	2
Supraventricular tachycardia	–	1	1
Miscellaneous	–	1	2

AVJ = atrioventricular junctional rhythm; PAC = premature atrial contraction; PVC = premature ventricular contraction.
* $p = 0.05$.

group was not significant, while this difference was highly significant in the retrospective group ($p < 0.001$). The results of the retrospective and prospective studies are compared in Table II. Before the operation, the prospective group showed significantly more arrhythmias than the retrospective group; we have no explanation for this. Postoperatively, the opposite was found; after modification of the cannulation technique the incidence and the severity of arrhythmias decreased significantly ($p < 0.05$).

24 Hour Holter recording.

Preoperative . Twenty–six out of 50 Holter recordings showed sinus rhythm throughout the 24–hour period. The abnormalities seen in the other 24 patients are listed in Table III. Seventeen children showed accelerated atrial rhythm during both nighttime and daytime. Children with accelerated atrial rhythm were older than children without, but the difference was not significant. Second–degree AV block was seen mainly, but not exclusively, during the nighttime.

Postoperative . Twenty–nine children showed sinus rhythm throughout the 24–hours period. Twenty–one children showed arrhythmias 3 months postoperatively, and 13 out of 46 had arrhythmias 1 year postoperatively (Table III). The percentage of children with accelerated atrial rhythm decreased gradually by 50% during follow–up ($p = 0.05$). Second–degree AV block was not seen after surgery. Two children had a short run of supraventricular

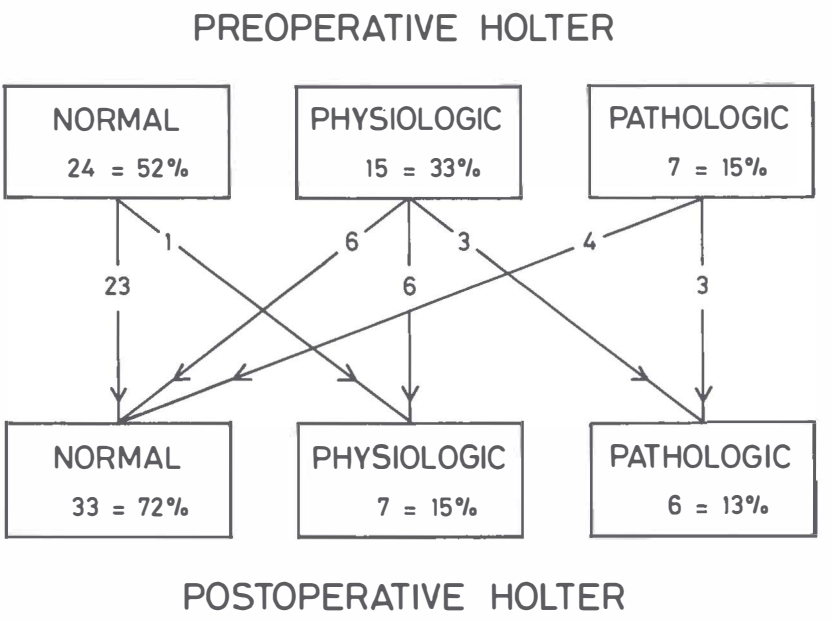

Fig. 1. Distribution of 46 patients according to their class of arrhythmias, as assessed by the 24–hour Holter recordings before and 1 year after ASD repair ($p < 0.05$).

tachycardia (SVT), one at 3 months and the other 1 year postoperatively. Neither of them became symptomatic during the further follow–up study. One boy with frequent PACs on the recording 1 year postoperatively had asymptomatic short runs of SVT on Holter recordings made 3 and 4 years postoperatively. Ten of 13 children with arrhythmias at 1 year had repeat Holter recordings during the years thereafter. These repeat recordings remained abnormal, but the condition did not deteriorate. The incidence of arrhythmias was not different for children with sinus venosus type of ASD, partial anomalous pulmonary venous drainage or fossa ovalis type of defect.

Many arrhythmias—e.g., atrial and AV junctional rhythm—found on the Holter recordings are also seen in children with normal hearts [11]. We divided the results of the Holter recordings into: (1) normal, i.e., only sinus rhythm; (2) "physiologic arrhythmias", i.e., also seen in healthy children; and (3) "pathologic arrhythmias" (Fig 1). After 1 year, only six children had "pathologic arrhythmias", three of these already had arrhythmias before their operation. The other three children with PACs and SVT developed these arrhythmias postoperatively. From the seven children with "pathologic arrhythmias" before operation, four had normal recordings after 1 year. As

mentioned before, 50% of the children with accelerated atrial rhythm had only sinus rhythm after 1 year of follow–up study. The difference between the pre– and postoperative distribution was significant ($p < 0.05$).

Exercise tests.

Exercise tests were performed postoperatively on 34 children. Eighteen children performed normally or above normal for their age and sex. The exercise level ranged from 75 to 133% (mean 96%) of normal. In two patients, PACs present at rest disappeared during exercise. None of the children developed arrhythmias during exercise.

DISCUSSION

The results of our previous retrospective study and the present prospective study show the importance of the venous cannulation method in preventing arrhythmias after an ASD repair. It seems likely that cannulation of the SVC through the RAA increases the risk of damage to the sinus node area and the sinus node artery directly or indirectly, by traction due to the weight of the cannula and the tubes or due to pulling at the cannula. Selective SVC cannulation leaves the sinus node and the sinus node artery untouched. Bharati and Lev [12] recently reported the autopsy findings of four patients who died suddenly, long after an ASD repair. Besides congenital malformations of the conduction system, surgical damage to the sinus node and fibrosis of the conduction tissue were found. It is possible that other factors played a role in our study. The change in cannulation technique alerted the surgeon even more than normal to avoid the sinus node area. The effect of this cannot be measured separately. We did not consider pump time and cardioplegia, because we found no significant correlation between these factors and the incidence of arrhythmias in our previous retrospective study.

In our retrospective study, 9 out of the 15 children who developed atrial flutter did this after the first year of follow–up (1.4–9.4 years postoperatively). Six of them already had other arrhythmias, mainly AV junctional rhythm, the first year postoperatively. We cannot exclude the possibility that some of the children in the prospective group will also develop atrial flutter after a longer follow–up period. It is well known from studies done after Mustard's operation and correction of tetralogy of Fallot, that arrhythmias can develop 10 to 15 years postoperatively. Therefore, the long–term significance of the change of cannulation has yet to be seen. We expect, however, that the total number of children with severe arrhythmias will remain smaller than in our former experience.

The decrease in first–degree AV block and accelerated atrial rhythm postoperatively suggests that ASD patients have preoperative abnormalities of conduction and automaticity. From our own electrophysiologic studies in preoperative ASD patients (to be published), and from the work of others [13–15], we know that the electrophysiologic parameters of the sinus node, the atrial myocardium, and the AV node are abnormal in many children with ASD. Our ECG findings could well be an expression of this phenomenon. It is likely that preoperative stretch of the atrial wall creates abnormal conduction and automaticity, which at an early age is reversible postoperatively.

Of the six children with "pathologic arrhythmias" 1 year postoperatively, three already had arrhythmias preoperatively. The other three children acquired their arrhythmias postoperatively. Postoperative arrhythmias, therefore, seem to be a combination of arrhythmias created by surgery and arrhythmias already present before surgery.

From our study we conclude that by direct cannulation of the SVC, instead of by indirect cannulation of it through the RAA, the incidence and severity of arrhythmias after an ASD repair can be reduced significantly (observations of a mean follow–up period of 2.6 years). Moreover, operating on children with ASD at an early age may diminish the incidence of arrhythmias present preoperatively.

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CHAPTER 7

GENERAL DISCUSSION AND CONCLUSIONS

GENERAL DISCUSSION AND CONCLUSIONS

Cardiac arrhythmias can develop after any type of atrial surgery. In this thesis we analyzed the arrhythmias seen after the Mustard operation for transposition of the great arteries and after closure of the atrial septal defect of the secundum type. Although the type of arrhythmias and their etiology are very alike, their severity, clinical consequences and the possibilities of prevention differ. Therefore, we decided to discuss the cardiac arrhythmias seen after the Mustard operation and the atrial septal defect repair separately.

In this chapter we will discuss the summarized results, the conclusions and the limitations of our studies. We will compare our findings with the recent literature and will discuss what implications our findings will have for the clinician and for future research.

Mustard operation for Transposition of the great arteries.

DISCUSSION OF THE RESULTS.

Although the methods and the periods of follow–up differ between the studies described in Chapters 2–4 [1–3], we found that the number of children with long–term sinus rhythm after a Mustard operation was only 40–50%, compared with 90–100% preoperatively. Moreover the percentage of children with sinus rhythm decreased with time, while the incidence of arrhythmias increased. Hayes and Gersony [4] had comparable results: the incidence of arrhythmias in their study increased gradually from 20% at the time of hospital discharge to 75% by the sixth year after operation. In contrast to the frequent loss of sinus rhythm, the atrioventricular conduction remained normal in all children of our study–group.

Considering the 90–100% incidence of sinus rhythm before operation, these arrhythmias must be caused by damage to the conduction system during surgery. Progressive fibrosis must account for the progression of the arrhythmias through the years. Many authors have discussed the etiology of these arrhythmias. Are they caused by damage to the sinus node or the sinus node artery, or by interruption of all atrial preferential pathways? The pathologists Edwards and Edwards [5] found fibrosis and degeneration of the sinus node, thrombosis and fibrosis of the sinus node artery, and fibrosis of the paranodal tissue in 77–100% (depending on the period of follow–up) of the children who died after a Mustard operation. Gillette and colleagues [6] found electrophysiologic proof of damage to the sinus node. Wittig and associates [7], performing intraoperative mapping at various stages of the Mustard procedure, found that a block of all preferential pathways resulted in an atrioventricular junctional rhythm. Saalouke et al. [8] concluded that damage to the sinus

node together with damage to the preferential pathways was responsible for the postoperative arrhythmias. In our study the type of arrhythmias and the results of our electrophysiologic testing showed the sinus node dysfunction. In addition, the prolonged refractory period in the atrium and the high incidence of induced supraventricular tachycardia are the consequences of electrophysiologic changes in the atrial myocardium. Recently Vetter and colleagues [9] published their results of endocardial mapping of the atrium after the Mustard operation. Besides severe sinus node dysfunction, they found intra–atrial conduction delay, dispersion of refractoriness and a 50% incidence of inducible atrial tachycardia. This combination of sinus node dysfunction, atrial conduction delay and abnormal refractoriness increases the risk of the development of reentrant tachycardias. On the other hand tachycardias can cause severe bradycardias by overdrive suppression of the sick sinus node.

We found that the incidence of postoperative arrhythmias decreased after the use of cardioplegia and selective cannulation (Chapter 2) [1]. The same improvement had earlier been found by El–Said and colleagues [10] in a comparison of their groups A and B. However, the longer follow–up of El–Said's original group B and the group C patients, who were operated upon with the same modifications, showed that this early beneficial effect of the surgical modifications disappeared with longer follow–up (Chapter 3) [2]. This was affirmed by the decrease in percentage of sinus rhythm seen after longer follow–up of the children operated on in Groningen, as described in Chapters 2 and 4 [1,3]. Although some centers [11,12] mentioned a much lower incidence of arrhythmias, it seems that the Mustard technique itself is, at least partially, responsible for the postoperative arrhythmias. This is mainly caused by the necessity to insert the patch close to the sinus node and to the excision of the atrial septum.

Besides severe electrophysiologic abnormalities, we found a high incidence of hemodynamic abnormalities, such as baffle obstructions and baffle leakage, in a group of asymptomatic children (Chapter 4) [3]. Some had to be reoperated or needed balloon angioplasty. Again, we found no improvement of the results after several surgical modifications. Dacron was used as baffle material in our group. Stark and associates [13] assumed that dacron was responsible for the high incidence of baffle obstructions, but the same was seen after use of pericardium [14].

The mean exercise tolerance of our children was 75% of normal, the ejection fraction of the right ventricle was borderline. There are indications that the heartrate response to exercise is diminished [15], and that the ejection fraction and the stroke volume do not increase, or even decrease, during

exercise in children after the Mustard operation [16,17]. This could point to an incapacity of the right ventricle to fully sustain the systemic circulation. This uneasiness about the long–term function of the right ventricle is confirmed by Warnes and Sommerville [18], who found right ventricular dysfunction and tricuspid regurgitation in 41% of patients with a mean period of 20 years after the Mustard operation.

The incidence of sudden death, which was significantly related to the presence of periods of atrial flutter, was very high in our series. Eight of the 11 children who died suddenly, died during exercise or proven tachycardia. Therefore the mechanism of sudden death is probably degeneration of atrial flutter with 1 : 1 conduction into ventricular fibrillation, and not a bradycardia–related death. Such an event has been described in a 22 year–old woman with Mustard correction and syncope [19]. This connection of atrial flutter and sudden death is in contrast with a recent prospective study of Deanfield et al., who saw sudden death in children without arrhythmias [20], but the connection is confirmed by others [21,22].

One of the limitations of our work is the retrospective character of the studies described in Chapters 2 and 3 [1,2]. The data could be biased, e.g. by the fact that possibly more electrocardiograms were taken in patients with arrhythmias and that these patients probably were seen more often in the center, while others were sent to local hospitals (Chapter 3) [2]. Late death by arrhythmias could have increased the percentage sinus rhythm of the remaining children. It seems probable, that such factors could explain the unexpected rise in the percentage of patients with sinus rhythm in group A. However, for group C we verified that the length of follow–up in the center did not differ between the children with and without arrhythmias.

Another subject of discussion can be the use of electrophysiologic tests to determine the sinus node function. This will be discussed in this chapter, in the section about the atrial septal defect. The abnormalities found during electrophysiologic testing after Mustard repair were so severe, that we feel free to use these abnormalities as proof of sinus node dysfunction in the majority of the children after the Mustard operation.

As in every institutional study that describes the effects of surgery, one has to bear in mind that the results cannot be generalized, although general patterns play a role. Surgery involves so much craft and skill, that results may differ greatly between surgeons.

CLINICAL IMPLICATIONS AND PERSPECTIVES.

The disappointing long–term results of the Mustard operation in our series appeal for an alternative surgical technique for children with transposition of the great arteries. The physiologic correction, as described by Senning (see Chapter 1), could be such an alternative. Turina and colleagues [23] published their long–term results of 220 survivors of the Senning procedure. Twelve per cent of the patients needed reoperation, 8% needed pacemaker implantation and 4% died suddenly. An electrophysiologic study performed by Byrum and associates [24] showed less sinus node dysfunction after the Senning operation than after the Mustard operation. Still, 3 out of 10 children had abnormal tests. Considering these data and the fact that the chance of progressive deterioration of right ventricular function is the same after the Senning operation as after the Mustard operation, we do not think the Senning technique a good alternative.

The arterial switch operation (see Chapter 1) had a very high mortality at first. In recent years the operative mortality decreased impressively. Quaegebeur et al. [25] had an early mortality of 12%, but only 3% in their last series, while Radley–Smith and Yacoub found a 9% mortality [26]. Late mortality was 5% and 0% respectively. A 20–institution cooperative study in 187 neonates with simple transposition, who underwent a Senning, Mustard or arterial switch operation, suggests that survival at 1 year is similar for all three types of operation [27]. However, one can expect that the late mortality after the arterial switch will be lower, considering the lower incidence of postoperative arrhythmias (see below). Mid–term results are encouraging, except for a 10% incidence of supravalvular pulmonary stenosis [28]. The incidence of arrhythmias is low [29]. Vetter and Tanner [30] performed the same electrophysiologic studies in children after an arterial switch operation, as they had earlier performed in children after a Mustard operation [9], and found only mild abnormalities of the sinus node and no abnormalities of the atrial myocardium, the atrioventricular node and the ventricle, except for a distal right bundle branch block in 9 out of 20 patients (repair of ventricular septal defect). The most important question for the future will be, whether the coronary arteries will develop normally. Wernovsky et al. [28] reported a proximal occlusion of the left anterior descending coronary artery in 2 children. Lösse and colleagues [31] found stress–induced, localized, myocardial ischemia in most children after the arterial switch operation.

Considering our disappointing long–term results of the Mustard operation, we prefer to perform the arterial switch operation in children with transposition, although the long–term results of this technique are not yet fully known.

Our study showed that after a Mustard operation children have to be followed carefully, with 24 hour Holter recording, 2–dimensional and Doppler echocardiography, and possibly cardiac catheterization, even if they seem to be doing well. Children with periods of atrial flutter are at high risk. Atrial anti–tachycardia pacing can possibly reduce the risk of sudden death [32].

It can be expected that in the future right ventricular dysfunction will become a problem in children or adults after a Mustard operation. In an effort to solve this problem, Mee [33] recently described the first results of a two–stage technique for patients with severe right heart failure after a Mustard or Senning operation. He performed a banding of the pulmonary artery, to create left ventricular hypertrophy, enough to provide for the systemic circulation. Much later he took out the atrial baffle and performed an arterial switch operation. Long–term results of this procedure have to be awaited.

Although the arrhythmias and electrophysiologic abnormalities after the arterial switch operation are of minor importance, the experience with the Mustard operation taught us to follow these children carefully and prospectively. It could well be, that the incidence of ventricular arrhythmias increases with time, which will certainly be the case if Lösse's [31] findings of areas of myocardial ischemia will be confirmed.

CONCLUSIONS.

— The incidence of arrhythmias after the Mustard operation is high (60%). The incidence of arrhythmias is directly related to the length of follow–up.

— The incidence of sudden death is very high (15%) in our group and significantly related to the presence of atrial flutter.

— Damage to the sinus node area combined with electrophysiologic alterations of the atrial myocardium is responsible for these arrhythmias.

— Surgical modifications only lead to an early improvement of the incidence of arrhythmias; the late results remain unfavorable.

— Even children, who are asymptomatic for a long time after the Mustard operation may have important hemodynamic and electrophysiologic abnormalities, despite the surgical modifications used.

— Given these results, we are in favor of replacing the physiologic correction, according to Mustard, by the arterial switch operation.

Atrial septal defect.

DISCUSSION OF THE RESULTS.

The incidence of arrhythmias after repair of the atrial septal defect is lower than after the Mustard operation, but still 10% of these children had severe arrhythmias that needed treatment. The type of arrhythmias was comparable; however, the consequences were less severe. Still one of the 204 children died suddenly and again this was a child that had experienced periods of atrial flutter since the operation. We did not perform electrophysiologic studies in children after repair of the atrial septal defect, but in view of the type of arrhythmias, we think that also in atrial septal defects, sinus node dysfunction and electrophysiologic abnormalities of the atrial myocardium are responsible for the arrhythmias. Apparently the damage to the conduction system is less extensive after the closure of an atrial septal defect than after the Mustard operation. In addition the myocardium of these non–cyanosed children probably tolerates fast ventricular rates during atrial flutter much better than the myocardium of children with transposition of the great arteries.

From our retrospective study we learned that the use of cardiopulmonary bypass increased the risk of postoperative arrhythmias (Chapter 2) [1]. The cannulation could be an important factor, causing damage to the sinus node or sinus node artery directly or indirectly. Clarkson and colleagues [34] had a similar finding in children who underwent a Mustard operation, with one or two cannula. Wittig and associates [7] found a shift of the functional pacemaker along the sulcus terminalis immediately after the cannulation. This shift was more often seen after cannulation through the right atrial appendage than after direct cannulation of the superior vena cava. Pathological evidence of damage to the sinus node was found by Bharati and Lev [35] in 4 patients who died suddenly, 2.5 months–9 years after repair of an atrial septal defect. Sutures and foreign body reaction to the sutures in addition to fibrosis were present in and around the sinus node, the atrial preferential pathways and the approaches of the atrioventricular node. Surgery was at least partially responsible for these abnormalities, but other factors played a role too, such as the preoperative abnormalities of the conduction system caused by the atrial septal defect itself.

The decrease in postoperative arrhythmias after the change in cannulation technique was rewarding (Chapter 6) [36]. The incidence of postoperative arrhythmias was about the same (electrocardiogram), or even less (24–hour Holter), than before operation. No severe symptomatic arrhythmias were seen. As discussed above, atrial flutter can develop a long time after operation. We have now followed this group for 2 more years, but none of them

has developed atrial flutter yet, while in the retrospective group, 13 of the 204 children developed atrial flutter within 3.6 years. The method of cannulation was the only change in technique between both studies, but we cannot be sure that this enormous improvement was caused by the change in cannulation only. The discussion about severe postoperative arrhythmias after a relatively "simple" operation, must have made the surgeons very alert in trying to avoid the sinus node area. This certainly has led to better results, but it does not change the conclusion, that arrhythmias after repair of the atrial septal defect can be prevented by surgical modifications.

The question remains why the incidence of supraventricular arrhythmias is higher after repair of an atrial septal defect than after other surgery, e.g. repair of a ventricular septal defect with the same cannulation technique. There could be two reasons for this. Firstly, in repair of an atrial septal defect, in addition to a possible injury of the sinus node by the cannulation, the atrial septum is sutured, which will result in fibrosis and changes in the conduction velocity and pattern. Secondly, the results of our electrophysiologic studies showed an abnormal electrophysiologic function of the sinus node and the atrial myocardium before operation (Chapter 5) [37]. Therefore, minor damage can probably result in arrhythmias. Electrophysiologic abnormalities were found in the majority of the children with atrial septal defect, but the abnormalities themselves were slight. Bolens and Friedli [38] found a clear improvement of the electrophysiologic values 5–12 weeks after operation. This is in agreement with the decrease in first–degree atrioventricular block and accelerated atrial rhythm in our group of children. Karpawich et al. [39] also found an improvement after surgery, but their electrophysiologic results remained abnormal 4–16 months after operation. However, it is very difficult to conclude from electrophysiologic studies which arrhythmias were already there before operation, and which were acquired by operation. Bolens and Friedli [38] found an improvement only in children who stayed in sinus rhythm after operation; 28% of their group acquired atrial ectopic rhythm as a result of surgery. The reversibility of preoperative arrhythmias is not found in adults. Although most adults improve clinically after surgical closure of their atrial septal defect, 88% of the patients with atrial fibrillation continued to have atrial fibrillation during the postoperative follow–up [40]. This suggests the importance of early surgical repair.

In our prospective study we had the opportunity to compare the preoperative and postoperative Holter recordings (Chapter 6) [36]. Thanks to the improvement of the surgical technique the abnormalities are less important after the operation than before. Three children developed arrhythmias, three

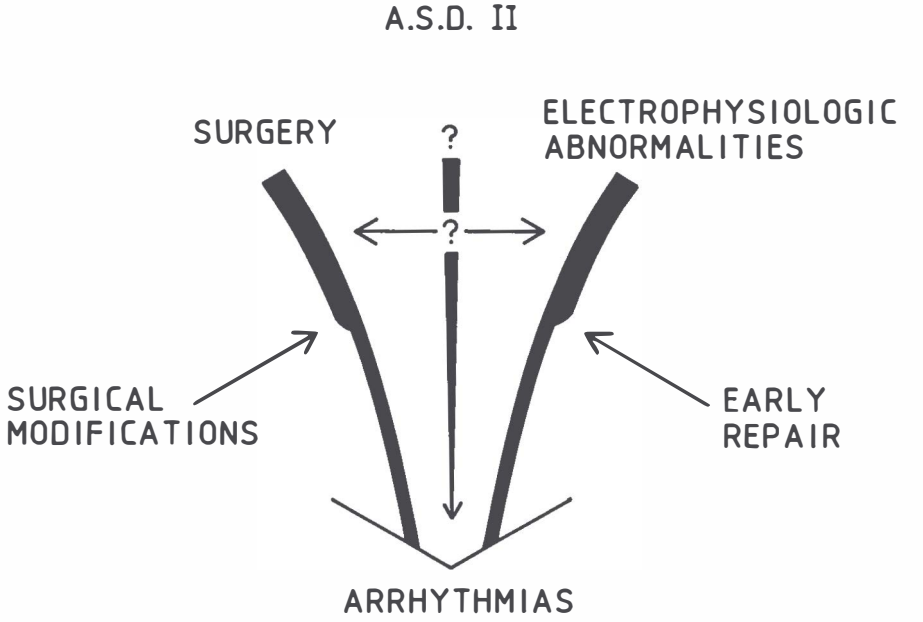

Fig. 1. Hypothesis of the development and prevention of arrhythmias after surgical closure of a secundum type atrial septal defect.

others kept their preoperative arrhythmias. However, the Holter recordings of these last three children became normal in the two years after the end of the study. The Holter recording of one of the children who acquired arrhythmias also became normal. Thus after longer follow–up, all preoperative "pathologic" arrhythmias disappeared, as did the majority of the "physiologic" arrhythmias. Two children still have "pathologic" arrhythmias, acquired after surgery, but they are asymptomatic.

Our hypothesis is (Fig.1.), that prolonged volume load creates arrhythmias and electrophysiologic abnormalities of the atrial myocardium and the adjacent conduction tissue. These arrhythmias and electrophysiologic abnormalities are probably reversible after surgery at a young age. These electrophysiologic alterations make the patient more susceptible to arrhythmias after surgery and will lead to supraventricular arrhythmias in adults with an unoperated atrial septal defect. On the other hand, surgical closure of an atrial septal defect can create arrhythmias, mainly by injuring the sinus node area. This can be prevented, for the most part, by surgical modifications, especially by selective cannulation of the superior vena cava.

One of the limitations of our study is that we compared the results of a retrospective study with the results of a prospective study. Investigation of two groups with standardized techniques, except for cannulation, would of course have been much more correct. However, we were so convinced of the negative influence of the cannulation, that in view of the incidence and the severity of the postoperative arrhythmias, we refrained from such a study for ethical reasons.

The value of electrophysiologic tests for the detection of sinus node dysfunction is a matter of discussion. Several studies found a low sensitivity and specificity, but all these studies were performed in adults [41]. Sinus node disease in adults is known to be a heterogeneous group of diseases. This could be one explanation for the lack of sensitivity and specificity. A group of children before or after operation for congenital heart disease is much more homogeneous; therefore, the results possibly have greater predictive value. The normal values used are the mean values + 2 SD, as found in children without clinical or electrophysiologic evidence of sinus node or atrial muscle disease [42]. Direct sinus node recording [43,44] would have given more precise information of the sinus node function, but this is still a difficult and time–consuming technique. Another factor influencing the results of electrophysiologic sinus node testing is the autonomic nervous system. Although all our children were sedated, individual changes in autonomic tone could have influenced our measurements. Pharmacological autonomic blockade would have been necessary to exclude these individual differences [45]. Despite these uncertainties and limitations, the sinus node recovery time and the sinoatrial conduction time are judged as clinically useful tests for sinus node dysfunction [46].

CLINICAL IMPLICATIONS AND PERSPECTIVES.

Considering the prevention of postoperative arrhythmias by selective cannulation of the superior vena cava, we would advise the use of this technique in all types of cardiac surgery. Although sinus node dysfunction is less common after other types of surgery, problems may also occur after other types of repair. In our own study of the conduction system after repair of Tetralogy of Fallot, we found a slightly or moderately prolonged sinus node recovery time in 18 out of 22 children (82%) and an abnormal sinoatrial conduction time in 15 out of 21 children (71%) (unpublished data).

We would advise to repair the atrial septal defect in asymptomatic children after the first year of life, and at any rate before the age of 4–5 years. Another argument for this, besides the arrhythmias and electrophysiologic abnormalities, is to be found in the study of Meyer and associates [47]. They found a

rapid dilatation of the right ventricle in the first 3 years of life due to the atrial shunt. In addition they found in 80% of the children that after repair, the right ventricle remained dilated many years after the operation. This can probably be prevented by repair of the atrial septal defect between 1 and 3 years of age.

Much work can still be done in the field of postoperative arrhythmias. One of the other atrial operations after which life–threatening arrhythmias are sometimes seen, is the Fontan operation. Prevention will be difficult to achieve, because the right atrial dilatation, inherent in the Fontan operation, predisposes to the development of supraventricular arrhythmias.

After ventricular surgery, e.g. the correction of Tetralogy of Fallot, 5% of the children die suddenly after a successful operation, probably by ventricular arrhythmias. Despite much research it is not totally clear which children are at risk, and not clear at all how these arrhythmias can be prevented. Prospective surgical trials with e.g. different suture material, repair through the atrium, younger age–groups etc. with careful follow–up including standardized electrophysiologic studies have to be done.

CONCLUSIONS.

— Children with atrial septal defect have preoperative arrhythmias and electrophysiologic abnormalities of the sinus node, the atrial myocardium, and the atrioventricular node.

— Arrhythmias after repair of the atrial septal defect partially consist of arrhythmias already present before operation and partially of arrhythmias acquired by surgery.

— The preoperative arrhythmias seem to disappear during the years after early operation.

— Surgical modifications, especially selective cannulation of the superior vena cava, significantly reduce the incidence and the severity of arrhythmias after the repair of the atrial septal defect.

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SUMMARY

SUMMARY

Thanks to the rapid development of cardiac surgery, the quality of life and the life expectancy of children with congenital heart disease has improved substantially during the last decades. However, one of the risks of cardiac surgery is that the conduction system of the heart, which is almost invisible for the surgeon, is damaged. This thesis deals with the cardiac arrhythmias seen after two types of operation in the atrium of the heart; the Mustard operation for transposition of the great arteries and the surgical repair of the atrial septal defect of the secundum type. The motive for the studies collected in this thesis was the fact that we saw a high incidence of arrhythmias after both operations, requiring drug treatment or pacemaker implantation, and occasionally resulting in sudden unexpected death. The objectives of our work were to determine the incidence, the severity and the natural history of the arrhythmias seen after these types of atrial surgery. An even more important goal was to detect the causes of these arrhythmias, and to find the starting–points for elimination of them. Chapter 1 gives the information essential for an understanding of the problem; information about the anatomy of the conduction system, the technique of the different operations, as well as the clinical consequences of injury of the conduction system.

In the study described in Chapter 2, we analyzed the arrhythmias seen after long–term follow–up in 50 children after the Mustard operation, and in 204 children after repair of an atrial septal defect. We found a 42% incidence of arrhythmias many years after the Mustard operation. The incidence of arrhythmias was influenced unfavorably by the cardio–pulmonary bypass time, and favorably by the use of cardioplegia and by selective cannulation of the superior vena cava. In patients with an atrial septal defect, the incidence of arrhythmias was less, but still 10% of the patients had severe arrhythmias, related to the type of atrial septal defect and the presence of partial abnormal venous drainage. The number of children with arrhythmias increased significantly, if cardio–pulmonary bypass was used instead of hypothermia. We wondered if the cannulation could have damaged the sinus node area directly or indirectly and thus causing arrhythmias. The incidence of sudden death was high in children after the Mustard operation and was significantly related to the presence of atrial flutter.

In 1974 the section of pediatric cardiology, Houston, USA, published their improved results after surgical modifications of the Mustard operation. Chapter 3 describes the longer follow–up of the patients operated upon in Houston with these modifications. Although the early results were favorable, long–term follow–up showed a progressive loss of sinus rhythm (50% after 5–8 years) and a gradual development of active and passive arrhythmias.

Although sudden death, reoperations and pacemaker implantations overshadow the results of the Mustard operation, most children are asymptomatic and do remarkably well. We studied 36 of these "asymptomatic" children hemodynamically and electrophysiologically, 7.7 ± 2.5 years after the operation and analyzed their electrocardiograms and 24–hour Holter recordings (Chapter 4). A surprising number of hemodynamic problems was found, such as systemic– and pulmonary venous baffle obstructions, baffle leakage and left ventricular outflow tract obstruction. Only 31% had no hemodynamic abnormalities. Moreover, the electrocardiogram showed sinus rhythm in only 42%, and only 6% of the children showed no abnormalities on their 24–hour Holter recording. Electrophysiologic studies revealed often severe sinus node dysfunction in 84%, and electrophysiologic abnormalities of the atrial myocardium in 63% of the children. In 32% of the children, supraventricular tachycardia was induced during the electrophysiologic study. The atrioventricular node function was normal in most children. There was no positive influence of the surgical modifications applied over the years.

In our general discussion (Chapter 7) we state that the sinus node area and the atrial myocardium are damaged by the Mustard operation, causing arrhythmias and sudden unexpected death by tachy–arrhythmias. This injury could not be prevented by several surgical modifications and seems to be inherent to the technique of the Mustard operation. Therefore, we advise to replace the Mustard operation by the arterial switch operation (Chapter 1), although the long–term results of this technique are not yet fully known.

In order to understand the relatively high incidence of arrhythmias after repair of an atrial septal defect, we undertook two further studies. First we performed an electrophysiologic study in 40 children with atrial septal defect preoperatively (Chapter 5). We found an abnormal electrophysiologic function of the sinus node in 83% of the children. The atrial myocardium also behaved abnormally. The electrophysiologic abnormalities of the atrioventricular node were less important. The electrocardiogram of 15% of the children showed first–degree atrioventricular block and 35% of the children had prolonged periods of accelerated atrial rhythm on their 24–hour Holter recording. Both abnormalities were significantly less frequent after repair of the atrial septal defect. It seemed reasonable that these electrophysiologic abnormalities and arrhythmias were the result of stretch of the right atrial wall and the adjacent conduction tissue by the prolonged volume load of the atrial septal defect. However, we could not find a correlation with age or shunt size in our group. This could be influenced by the fact that we had to exclude the data of 11 young patients, whose sinus node measurements appeared to be influenced by premedication with thiopental.

Analysis of the 24–hour Holter recordings of 46 children before, and one year after, atrial septal defect operation (Chapter 6) showed that arrhythmias seen after operation partially consist of arrhythmias already present before operation and partially of arrhythmias acquired as a result of the operation. The arrhythmias present before operation tended to disappear in the years after repair of the atrial septal defect. This is not seen after operation of an atrial septal defect in adults.

The results of our former retrospective study (Chapter 2) showed that cannulation could possibly be responsible for the injury of the sinus node area. Therefore, our second study in patients with an atrial septal defect (Chapter 6) was a prospective study in 50 children, who were operated upon with a change in cannulation technique. The superior vena cava was cannulated directly instead of through the right atrial appendage. The incidence of postoperative arrhythmias decreased significantly from 23 to 10%. Moreover, no severe arrhythmias (e.g atrial flutter) were seen during long–term follow–up of the prospective group, compared with 10% in the retrospective group.

In our general discussion (Chapter 7) we state that arrhythmias after surgical repair of atrial septal defect partially consist of arrhythmias present before operation and partially of arrhythmias caused by the operation. Early repair of atrial septal defect probably will increase the chance that the electrophysiologic abnormalities and arrhythmias, present before operation, will disappear after operation. Moreover, the development of arrhythmias after surgical repair of an atrial septal defect can be reduced significantly by surgical modifications, such as selective cannulation of the superior vena cava. We suggest that this cannulation technique be used in all types of cardiac surgery.

These studies show that early prospective studies should be done after every new type of cardiac surgery to analyze the causal factors of arrhythmias and to find methods of prevention.

SAMENVATTING

SAMENVATTING

Dankzij de ontwikkeling van de hartchirurgie is de levenskwaliteit en de levensverwachting van kinderen met een aangeboren hartafwijking in de laatste decennia indrukwekkend verbeterd. Eén van de risico's van hartchirurgie is echter dat tijdens de operatie het, voor de chirurg grotendeels onzichtbare, geleidingssysteem wordt beschadigd. Wij bestudeerden in dit proefschrift de gevolgen voor het geleidingssysteem van twee veel uitgevoerde operaties in de boezems van het hart: 1. de Mustard operatie bij kinderen met een transpositie van de grote arteriën en 2. de chirurgische sluiting van het atrium septum defect type II. De aanleiding voor dit onderzoek was het feit dat bij kinderen na deze operaties vaak supraventriculaire ritmestoornissen optraden, die medicamenteuze behandeling of pacemaker implantatie noodzakelijk maakten. Bovendien overleden enige kinderen acuut jaren na een ogenschijnlijk geslaagde operatie, vermoedelijk op basis van deze ritmestoornissen. Het doel van de studies, die in dit proefschrift staan beschreven, was het inventariseren van het aantal, de ernst en het verloop van de ritmestoornissen na deze beide operaties. Een nog belangrijker doel was het zoeken naar de oorzaken van deze ritmestoornissen en het vinden van mogelijkheden om deze te voorkomen. In Hoofdstuk 1 wordt de informatie gegeven, die nodig is om de problematiek te verduidelijken; de anatomie van het geleidingssysteem, de techniek van de verschillende operaties en de klinische gevolgen van beschadiging van het geleidingssysteem.

In het onderzoek beschreven in Hoofdstuk 2 wordt de frequentie van voorkomen en de ernst van de ritmestoornissen onderzocht bij 50 kinderen, die een Mustard operatie hebben ondergaan en bij 204 kinderen, waarbij het atrium septum defect chirurgisch is gesloten. Vele jaren na de Mustard operatie bleek 42 procent van de kinderen ritmestoornissen te hebben. Het percentage ritmestoornissen werd ongunstig beinvloed door een lange perfusietijd en gunstig door het gebruik van cardioplegie tijdens de operatie en door selectieve canulatie van de vena cava superior. Na operatie van een atrium septum defect hadden minder kinderen ritmestoornissen, maar nog altijd had 10% van hen ernstige ritmestoornissen, waarvoor behandeling nodig was. De ligging van het atrium septum defect en de aanwezigheid van een partiële abnormale longvenen drainage hadden een significante invloed op het percentage ritmestoornissen. Opvallender was, dat het percentage ritmestoornissen significant veel hoger was wanneer de hart–long machine werd gebruikt dan wanneer zonder hart–long machine onder hypothermie werd geopereerd. Wij vroegen ons af of mogelijk bij de canulatie de sinusknoop en/of de sinusknoop arterie direct of indirect werden beschadigd. Na de Mustard operatie werd bovendien een hoge incidentie van acute hartdood gezien. Acute

hartdood trad significant vaker op bij kinderen, die periodiek of continu atriumfladderen vertoonden.

In 1974 publiceerde de afdelig kindercardiologie, Houston USA, dat de resultaten na de Mustard operatie waren verbeterd na een aantal modificaties van de chirurgische techniek. In Hoofdstuk 3 worden de resultaten op langere termijn beschreven van de patienten, die in Houston geopereerd werden met de gemodificeerde techniek. Het bleek dat, alhoewel de eerste resultaten gunstig waren, de patienten toch in de loop der jaren progressief ritmestoornissen ontwikkelden, en dat na 5–8 jaar nog slechts 50% van de groep een normaal sinusritme had.

Hoewel na de Mustard operatie acute hartdood voorkomt en soms reoperatie en pacemaker implantatie nodig is, maakt het merendeel van de kinderen het goed en doet normaal met hun leeftijdsgenootjes mee. Wij verrichtten bij 36 van deze "asymptomatische" kinderen, gemiddeld 7,7 ± 2,5 jaar na de operatie, een hartcatheterisatie teneinde eventuele verborgen hemodynamische of electrofysiologische afwijkingen op het spoor te komen (Hoofdstuk 4). Tevens werden van alle kinderen de electrocardiogrammen en 24–uur's electrocardiogrammen geanalyseerd. Vele kinderen bleken een obstructie van de baffle te hebben bij de inmonding van de systeem– of longvenen. Ook baffle–lekkage en obstructie van de uitgang van de linker kamer werden frequent gevonden. Slechts 31% van de kinderen had geen hemodynamische afwijkingen. Van de kinderen was nog maar 42% in sinusritme, terwijl slechts 6% een normaal 24–uur's electrocardiogram had. Electrofysiologisch onderzoek bracht, bij 84% van de kinderen, vaak ernstige, afwijkingen van de sinusknoop aan het licht. Het merendeel had tevens electrofysiologische afwijkingen van het boezemmyocard. Bij 32% van de kinderen kon door middel van electrische stimulatie van het hart een supraventriculaire tachycardie worden opgewekt. Alleen de atrioventriculaire knoop functioneerde vrijwel steeds normaal. Wij zagen geen positief effect van de in de loop der jaren aangebrachte veranderingen in chirurgische techniek.

Wij stellen in de algemene discussie in Hoofdstuk 7, dat zowel de sinusknoop met zijn omgeving als het boezemmyocard door de Mustard operatie worden beschadigd, hetgeen leidt tot ritmestoornissen en soms tot acute hartdood door tachy–aritmieën. Deze beschadiging is onverminderd blijven bestaan, ondanks allerlei veranderingen in de chirurgische techniek en lijkt inherent te zijn aan de techniek van de Mustard operatie zelf. Wij adviseren daarom de Mustard operatie te vervangen door de "arteriële switch operatie" (Hoofdstuk 1), ook al zijn de lange termijn resultaten van deze operatie nog niet volledig bekend.

Teneinde te begrijpen waarom na de operatie van een atrium septum defect relatief veel ritmestoornissen voorkomen, werden twee studies verricht. In de eerste studie werd bij 40 kinderen met een ASD, die nog niet geopereerd waren, een electrofysiologisch onderzoek verricht (Hoofdstuk 5). Het bleek dat bij 83% van de kinderen de sinusknoop electrofysiologisch abnormaal functioneerde. Ook het boezemmyocard toonde bij veel kinderen electrofysiologische afwijkingen. De afwijkingen van de atrioventriculaire knoop waren geringer. Vijftien procent van de kinderen had een eerste graads atrioventriculair blok en 35% van de kinderen had lange periodes versneld boezemritme in hun 24–uur's electrocardiogram. Beide afwijkingen werden ná de operatie significant minder vaak gezien. Het lijkt waarschijnlijk, dat deze electrofysiologische afwijkingen en ritmestoornissen het gevolg zijn van rek van de rechter boezemwand en het aangrenzende geleidingsweefsel, veroorzaakt door de langdurige volumebelasting van het atrium septum defect. Wij konden echter in onze groep geen verband vinden tussen de aanwezigheid van electrofysiologische afwijkingen en ritmestoornissen enerzijds en leeftijd en shuntgrootte anderzijds. Mogelijk speelt hierbij een rol dat wij de gegevens van 11 jonge kinderen niet konden gebruiken, omdat de premedicatie met thiopental de electrofysiologische metingen bleek te hebben beinvloed.

Analyse van de 24–uur's electrocardiogrammen gemaakt vóór en 1 jaar ná operatie bij 46 kinderen (Hoofdstuk 6) liet zien, dat de postoperatieve ritmestoornissen deels bestonden uit ritmestoornissen, die vóór de operatie al aanwezig waren en deels uit ritmestoornissen, die ná de operatie waren ontstaan. De preoperatieve ritmestoornissen hadden de neiging te verdwijnen in de jaren na de operatie van het atrium septum defect. Dit is in tegenstelling met wat gezien wordt bij patienten, die op volwassen leeftijd worden geopereerd.

De resultaten van het retrospectieve onderzoek (Hoofdstuk 2) wezen erop, dat de canulatie mogelijk verantwoordelijk was voor de beschadiging van de sinusknoop en omgeving. Daarom was onze tweede studie bij patienten met een atrium septum defect (Hoofdstuk 6) een prospectief onderzoek bij 50 kinderen, die geopereerd werden met een andere canulatietechniek. De vena cava superior werd nu niet meer vanuit het rechter hartoor gecanuleerd maar rechtstreeks. Het aantal kinderen met ritmestoornissen na de operatie daalde significant van 23 naar 10%. Belangrijker was dat niemand ernstige ritmestoornissen ontwikkelde, in tegenstelling tot 10% in de retrospectieve groep.

In de algemene discussie (Hoofdstuk 7) stellen wij dat ritmestoornissen na operatieve sluiting van een atrium septum defect, deels bestaan uit ritmestoornissen die tevoren reeds aanwezig waren en deels uit ritmestoornissen die ná de operatie zijn ontstaan. Operatieve sluiting van het atrium septum defect op jonge leeftijd zal waarschijnlijk de kans vergroten, dat de preoperatief aanwezige ritmestoornissen ná de operatie verdwijnen. De kans op het

ontstaan van ritmestoornissen ná de operatie van een atrium septum defect kan significant worden verkleind door veranderingen in de chirurgische techniek, met name door selectieve canulatie van de vena cava superior. Wij adviseren dan ook deze canulatietechniek eveneens bij andere types hartoperaties toe te passen.

Wij leerden van de studies, beschreven in dit proefschrift, dat bij ieder nieuw type hartoperatie vroeg en prospectief onderzoek verricht moet worden, teneinde eventuele oorzaken van ritmestoornissen op het spoor te komen, zodat in een vroeg stadium preventieve maatregelen genomen kunnen worden.

SAMENVATTING VOOR DE NIET MEDICUS

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Aangeboren hartafwijkingen komen voor bij 0,8% van de pasgeborenen. Sommige afwijkingen zijn zo gering, dat chirurgische behandeling niet noodzakelijk is. Andere afwijkingen hebben echter op korte of langere termijn een negatieve invloed op de levensverwachting of de levenskwaliteit. Dankzij de snelle ontwikkeling van de hartchirurgie sinds 1938, zijn er voor het merendeel van deze afwijkingen nu operatieve mogelijkheden. Hierdoor is het perspectief voor kinderen met een aangeboren hartafwijking indrukwekkend verbeterd.

Eén van de risico's van hartchirurgie is echter dat het, voor de chirurg vrijwel onzichtbare, geleidingssysteem wordt beschadigd. Via dit geleidingssysteem wordt vanuit de sinusknoop de electrische prikkel, die het hart tot samentrekken aanzet, naar de boezems en via de atrioventriculaire (AV) knoop naar de kamers geleid. Schade aan dit geleidingssysteem leidt tot ontregeling van de hartslag. Dit uit zich in een te langzame hartslag (bradycardie) of juist een ongecontroleerd snelle hartslag (tachycardie) of de combinatie van beide.

Wij bestudeerden in dit proefschrift de gevolgen voor het geleidingssysteem van twee veel uitgevoerde operaties in de boezems van het hart: 1. de Mustard operatie, gebruikt bij kinderen waarbij de slagaders tijdens de aanleg verkeerd op het hart zijn aangesloten (transpositie van de grote arteriën) en 2. de chirurgische sluiting van een defect in de boezemtussenwand (atrium septum defect, ASD). De aanleiding voor dit onderzoek was het feit dat bij kinderen na deze operaties vaak een ontregeling van de hartslag optrad, die behandeling met medicijnen of implantatie van een electrische gangmaker (pacemaker) noodzakelijk maakte. Bovendien overleden enige kinderen acuut jaren na een ogenschijnlijk geslaagde operatie, vermoedelijk op basis van deze ritmestoornissen. Het doel van de in dit proefschrift verzamelde studies, was het inventariseren van het aantal, de ernst en het verloop van de ritmestoornissen na deze operaties. Een nog belangrijker doel was het zoeken naar de oorzaken van deze ritmestoornissen en het vinden van mogelijkheden om deze te voorkómen. In Hoofdstuk 1 wordt de informatie gegeven, die nodig is om de problematiek te verduidelijken; de anatomie van het geleidingssysteem, de techniek van de verschillende operaties en de klinische gevolgen van beschadiging van het geleidingssysteem.

In Hoofstuk 2 wordt een onderzoek beschreven bij 50 kinderen, die een Mustard operatie hadden ondergaan en 204 kinderen, waarbij een atrium septum defect was gesloten, met als doel de frequentie van vóórkomen, de ernst en het verloop van eventuele ritmestoornissen te leren kennen. Vele jaren na de Mustard operatie bleek 42% van de kinderen ritmestoornissen te hebben. De incidentie van ritmestoornissen werd ongunstig beinvloed door de

tijdsduur van de operatie en gunstig door een bepaalde bescherming met medicijnen (cardioplegie) van de hartspier tijdens de operatie en door een andere manier van inbrengen van de canule van de hart–long machine in de bovenste holle ader (vena cava superior, SVC). Na operatie van een atrium septum defect hadden minder kinderen ritmestoornissen, maar nog altijd had 10% van hen ernstige ritmestoornissen, waarvoor behandeling nodig was. Het ontstaan van deze ritmestoornissen hing o.a. samen met de plaats van het defect in de boezemtussenwand. Opvallender was, dat het percentage ritmestoornissen significant veel hoger was wanneer de hart–long machine werd gebruikt, dan wanneer zonder hart–long machine werd geopereerd. Wij vroegen ons af of bij de canulatie van de bovenste holle ader de dichtbij gelegen sinusknoop en/of sinusknoopslagader direct of indirect werden beschadigd, met als gevolg ritmestoornissen. Na de Mustard operatie werd bovendien een hoge incidentie van acute hartdood gezien. Acute hartdood trad significant vaker op bij kinderen met één bepaald soort boezemtachycardie.

In 1974 publiceerde de afdeling kindercardiologie, Houston USA, dat de resultaten van de Mustard operatie waren verbeterd na een aantal modificaties van de chirurgische techniek. In Hoofdstuk 3 worden de resultaten op langere termijn beschreven van de patienten, die in Houston geopereerd werden met de gemodificeerde techniek. Het bleek dat, alhoewel de eerste resultaten gunstig waren, de patienten toch in de loop der jaren progressief ritmestoornissen ontwikkelden, en dat na 5–8 jaar nog slechts 50% van de groep normaal (sinus) ritme had.

Hoewel na de Mustard operatie acute hartdood voorkomt en soms reoperatie of pacemakerimplantatie nodig is, maakt het merendeel van de kinderen het goed en doet normaal mee met hun leeftijdsgenootjes. Wij onderzochtten 36 van deze klachtenvrije kinderen, gemiddeld 7,7 jaar na de operatie, op eventuele verborgen afwijkingen. Wij deden dit door middel van een hartcatheterisatie, waarbij tevens (electrofysiologisch) onderzoek naar de conditie van het geleidingssysteem werd verricht (Hoofdstuk 4). Het bleek dat slechts 31% van de kinderen een goed operatieresultaat had. Het merendeel toonde vernauwingen of een lekkage van de jaren tevoren in het hart aangebrachte kunststof "tunnel". Bovendien werden bij velen ernstige electrofysiologische afwijkingen van de sinusknoop en van de boezemspierwand gevonden. Deze afwijkingen waren ook zichtbaar in het electrocardiogram (ECG) en het 24–uur's electrocardiogram van de kinderen. Ondanks de in de loop van de tijd aangebrachte veranderingen in de chirurgische techniek werden geen significante verbeteringen gezien.

Wij stellen in de algemene discussie in Hoofdstuk 7, dat zowel de sinusknoop met zijn omgeving als de boezemspierwand door de Mustard operatie worden beschadigd, met als gevolg ritmestoornissen en soms acute hartdood.

Deze beschadiging is onverminderd blijven bestaan, ondanks allerlei veranderingen in de chirurgische techniek en lijkt inherent te zijn aan de techniek van de Mustard operatie zelf. Wij adviseren daarom de Mustard operatie te vervangen door de "arteriële switch operatie" (Hoofdstuk 1), ook al zijn de lange termijn resultaten van deze operatie nog niet volledig bekend.

Teneinde te begrijpen waarom na de operatieve sluiting van een atrium septum defect relatief veel ritmestoornissen voorkomen werden twee studies verricht. In de eerste studie werd bij 40 kinderen met een atrium septum defect, die nog niet geopereerd waren, een electrofysiologisch onderzoek verricht (Hoofdstuk 5). Het bleek dat bij het merendeel de sinusknoop electrofysiologisch abnormaal functioneerde, evenals de spierwand van de boezem. Vele kinderen bleken ook, zij het lichte, ritmestoornissen te hebben in hun electrocardiogram en 24–uur's electrocardiogram. Ná de operatie namen deze ritmestoornissen in aantal af. Het lijkt waarschijnlijk, dat deze electrofysiologische afwijkingen en ritmestoornissen het gevolg zijn van rek van de rechter boezemwand en het aangrenzende geleidingsweefsel, veroorzaakt door de langdurige volumebelasting via het defect in de boezemtussenwand. Wij konden echter in onze groep geen verband vinden tussen de aanwezigheid van electrofysiologische afwijkingen en ritmestoornissen enerzijds en de leeftijd en de grootte van de links–rechts shunt via het atrium septum defect anderzijds. Mogelijk speelt hierbij een rol dat wij de gegevens van 11 jonge kinderen niet konden gebruiken, omdat de gegeven premedicatie de electrofysiologische metingen bleek te hebben beinvloed.

Analyse van de 24–uur electrocardiogrammen gemaakt vóór en 1 jaar ná operatie bij 46 kinderen (Hoofdstuk 6) liet zien, dat de postoperatieve ritmestoornissen deels bestonden uit ritmestoornissen, die vóór de operatie al aanwezig waren en deels uit ritmestoornissen, die ná de operatie waren ontstaan. De preoperatieve ritmestoornissen hadden de neiging te verdwijnen in de jaren ná de operatie van het atrium septum defect. Dit is in tegenstelling met wat gezien wordt bij patienten, die op volwassen leeftijd worden geopereerd.

De resultaten van het retrospectieve onderzoek (Hoofdstuk 2) wezen erop, dat de canulatie, met name het inbrengen van de canule van de hart–long machine in de bovenste holle ader, mogelijk verantwoordelijk was voor de beschadiging van de sinusknoop en omgeving. Daarom was onze tweede studie bij patienten met een atrium septum defect (Hoofdstuk 6) een prospectief onderzoek bij 50 kinderen, die geopereerd werden met een andere canulatietechniek. De bovenste holle ader werd nu niet meer vanuit de rechter boezem gecanuleerd, maar rechtstreeks. Het aantal kinderen met ritmestoornissen na de operatie daalde significant van 23 naar 10%. Belangrijker was, dat

niemand ernstige ritmestoornissen ontwikkelde, in tegenstelling tot 10% in de retrospectieve groep.

In de algemene discussie (Hoofdstuk 7) stellen wij dat ritmestoornissen na de operatieve sluiting van een atrium septum defect deels bestaan uit ritmestoornissen die tevoren al aanwezig waren en deels uit ritmestoornissen, die ontstaan zijn ná de operatie. Operatieve sluiting van het atrium septum defect op jonge leeftijd zal de kans vergroten, dat de preoperatieve ritmestoornissen na de operatie verdwijnen. De kans op het ontstaan van ritmestoornissen ná operatie van een atrium septum defect kan significant worden verkleind door veranderingen in de chirurgische techniek, met name door selectieve canulatie van de bovenste holle ader. Wij adviseren dan ook deze canulatietechniek eveneens bij andere types hartoperaties toe te passen.

Wij leerden van de studies, beschreven in dit proefschrift, dat bij ieder nieuw type hartoperatie vroeg en prospectief onderzoek verricht moet worden, teneinde eventuele oorzaken van ritmestoornissen op het spoor te komen, zodat in een vroeg stadium preventieve maatregelen genomen kunnen worden.

LIST OF ABBREVIATIONS

2-D	2-Dimensional
AF	Atrial flutter
ASD	Atrial septal defect
AV	Atrioventricular
AVJ	Atrioventricular junctional
CSNRT	Corrected sinus node recovery time
ECG	Electrocardiogram
IVC	Inferior vena cava
PAC	Premature atrial contraction
PVC	Premature ventricular contraction
QP	Pulmonary blood flow
QS	Systemic blood flow
RA	Right atrium
RAA	Right atrial appendage
SA	Sinoatrial
SACT	Sinoatrial conduction time
SD	Standard deviation
SND	Sinus node dysfunction
SNRT	Sinus node recovery time
SVC	Superior vena cava
SVT	Supraventricular tachycardia
VSD	Ventricular septal defect